Johnson & Johnson Vision Care, Inc.

Clinical Study Protocol

Ocular Characteristics in Contact Lens and Spectacle Wear

Protocol: CR-6332

Version: 4.0, Amendment 3.0

Date: 16 April 2019

Investigational Products: ACUVUE OASYS®1-Day with HydraLuxe™ Technology (senofilcon A)

Key Words: Senofilcon A, ACUVUE OASYS® 1-Day with HydraLuxe™ Technology, daily disposable, daily wear, dispensing, symptomatic, characterization, CLDEQ-8, DEQ-5, Spectacle, Sensitivity Questionnaire (Highly Sensitive Person-HSP Scale), Meibomian Gland Expressibility, Meibomian Gland Evaluator (MGE), blink patterns, tear film stability (NIBUT/NIKBUT), lid wiper epitheliopathy, conjunctival staining

Statement of Compliance to protocol, GCP and applicable regulatory guidelines:
This trial will be conducted in compliance with the protocol, ISO 14155,[1] the International Conference on Harmonization Good Clinical Practice E6 (ICH-GCP),[2] the Declaration of Helsinki,[3] and all applicable regulatory requirements.

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PROTOCOL TITLE, NUMBER, VERSION

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SPONSOR NAME AND ADDRESS

Johnson & Johnson Vision Care (JJVC)
7500 Centurion Parkway
Jacksonville, FL 32256

MEDICAL MONITOR

Name: Elizabeth Dow, OD, FAAO
Title: Principal Research Optometrist
Address: 7500 Centurion Parkway, Suite 100; Jacksonville, FL 32256
[redacted]
Email: edow1@its.jnj.com
[redacted]
The Medical Monitor must be notified by the clinical institution/site by e-mail, fax, or telephone within 24 hours of learning of a Serious Adverse Event. The Medical Monitor may be contacted during business hours for adverse event questions. General study related questions should be directed towards your assigned clinical research associate.

The Medical Monitoring Plan is maintained as a separate document and included in the Trial Master File.

AUTHORIZED SIGNATURES

The signature below constitutes the approval of this protocol and the attachments, and provides the necessary assurances that this trial will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable U.S. federal regulations,[4] ICH guidelines,[2] ISO 14155,[1] and the Declaration of Helsinki.[3]

Author & Study Responsible Clinician	**See Electronic Signature Report** Elizabeth Dow, OD, FAAO Principal Research Optometrist, R&D	DATE
Clinical Operations Manager	**See Electronic Signature Report** [redacted] Clinical Operations Manager, Clinical Operations	DATE
Biostatistician	**See Electronic Signature Report** [redacted] Biostatistician, Clinical Sciences, R&D	DATE
Biostatistics Reviewer	**See Electronic Signature Report** [redacted] Sr Biostatistics Manager, R&D	DATE
Data Management	**See Electronic Signature Report** [redacted] Clinical Project Manager – Data & Systems, Clinical Operations	DATE
Fellow Reviewer	**See Electronic Signature Report** [redacted] Research Fellow, R&D	DATE
Approver	**See Electronic Signature Report** [redacted] Director, Sphere-Light Management-Lens Care, JJVC	DATE

CHANGE HISTORY

Version	Originator	Description of Change(s) and Section Number(s) Affected	Date
1.0	Elizabeth Dow	Original Protocol	15 MAR 2019
2.0	Elizabeth Dow	Visits 1 & 3 exit acuity: updated from LogMAR to Snellen Updated Table 2: Distance Powers Updated Supplies Table: GreenGlo [redacted]	20 MAR 2019
3.0	John Peterson	Added "as applicable" to Table 1 [redacted] Updated PRO Specs. MIS01741 Response Set	05 APR 2019
4.0	Elizabeth Dow	Corrected "LogMAR" to "Snellen" in step 3.24 Corrected "transition" to "photochromic" in Exclusion Criteria 7 & Step 1.4 [redacted] (Step 1.23 & Appendix D)	16 APR 2019

SYNOPSIS

Protocol Title	Ocular Characteristics in Contact Lens and Spectacle Wear
Sponsor	JJVC, 7500 Centurion Parkway, Jacksonville, FL 32256
Clinical Phase	Post Marketing (Marketing claims, registry, post marketing surveillance), phase 4
Trial Registration	This study will be registered on ClinicalTrials.gov by the Sponsor
Test Article(s)	Investigational Products: Test: ACUVUE OASYS ® 1-Day with Hydraluxe™ Technology Control: Subject's own Spectacle
Wear and Replacement Schedules	Wear Schedule: Daily Wear Replacement Schedule: Daily Disposable
Objectives	Primary Objective(s): Compare between Test lens and Spectacles with respect to non-invasive break up time (NIBUT)/ non-invasive keratography break up time (NIKBUT) among habitual lens users. Secondary Objective(s): Compare between Test lens and Spectacles with respect to Meibomian gland expressibility, conjunctival staining, and lid wiper epitheliopathy among habitual lens users. Other Objective(s): Compare between Test lens and Spectacles among habitual lens users with respect to digital device ocular symptoms, digital device use, blink characteristics, and subjective sensitivity. The same comparisons presented above will be conducted between Spectacles/Test lens for habitual contact lens users and Spectacles for habitual spectacle users.
Study Endpoints	Primary endpoint(s): Non-invasive break up time (NIBUT)/ non-invasive keratography break up time (NIKBUT) time in seconds (Appendix E and Appendix F) Secondary endpoint(s): • Meibomian gland expressibility (Appendix I) • Conjunctival staining [redacted] • Lid wiper epitheliopathy (Appendix H)

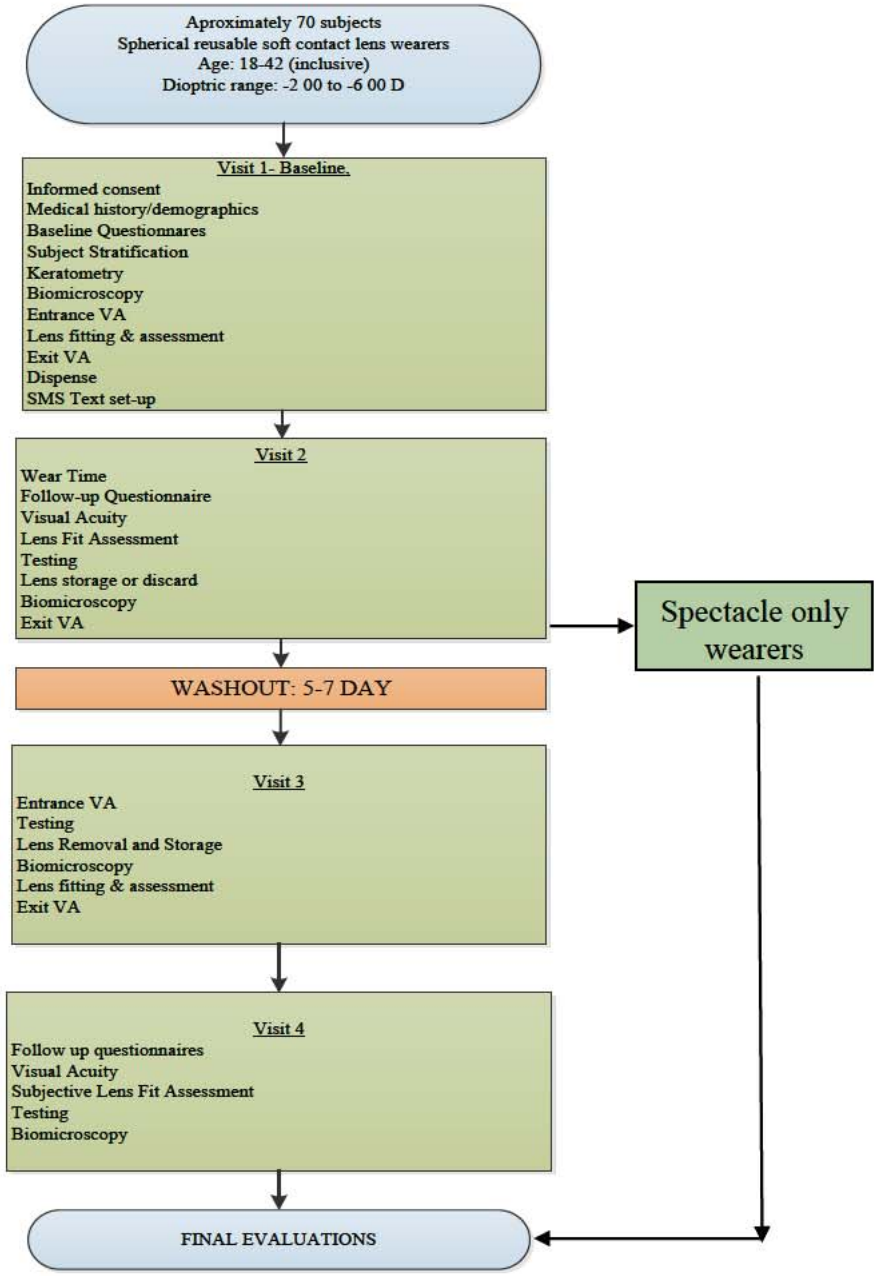
	Other exploratory endpoint(s): • Dry eye symptoms assessed by time point modified CLDEQ-8/DEQ-5 [redacted] • Subjective comfort assessed by (0-100) numeric scale • Digital device use and the related ocular symptoms assessed by digital device use and ocular symptoms surveys • Blink characteristics • Subjective sensitivity measured by Highly Sensitive Person-HSP Scale
Study Design	This is a two-arm study. There will be an observational arm and an interventional arm. In the observational arm, habitual spectacle wearers will all continue to use their habitual optical correction and undergo ocular evaluations and questionnaires at 2 separate study visits. The observational arm will have a total of 2 visits: Visit 1: Screening, baseline evaluation Visit 2: Follow up evaluation and final evaluation. In the interventional arm, habitual contact lens wearers who own spectacles will undergo a bilateral, dispensing, randomized, controlled, unmasked, 2×2 cross-over study over 4 visits. Each subject will be bilaterally fitted with the one test article and crossed with their own spectacle in 2 periods. The interventional arm will have a total of 4 visits: Visit 1: Screening, baseline evaluation, randomization to lens fit or spectacle wear × 1 week. Visit 2: Follow-up evaluation WASHOUT: 1 week Visit 3: Lens fit or spectacle wear × 1 week. Visit 4: Follow-up evaluation and final evaluation. See the flow chart at the end of the synopsis table for the schematic of the study visits and procedures of main observations (Figure 1).
Sample Size	Approximately 70 eligible subjects are to be enrolled and 60 subjects are needed to complete
Study Duration	The study is anticipated to last 6 weeks and include a 2 week enrollment period.
Anticipated Study Population	40 habitual soft contact lens users, and 20 non contact lens using spectacle wearers, between 18-42 years of age (inclusive)
Eligibility Criteria	Potential subjects must satisfy all of the following criteria to

	be enrolled in the study: Inclusion Criteria after Screening 1. The subject will have completed the pre-screening Classification questionnaire. 2. Subject must have a working cell phone capable of sending and receiving text messages. 3. The subject must read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form. 4. Appear able and willing to adhere to the instructions set forth in this clinical protocol 5. Between 18 and 42 (inclusive) years of age at the time of screening 6. Be a current soft contact lens wearer in both eyes with a minimum of 5 days/week wear time over the last 1 month by self-report OR be a full time spectacle wearer (7 days/ week) without contact lens wear over the last 6 months 7. Subjects must be willing to adhere to spectacle-only refractive correction for approximately 1 week Inclusion Criteria after Baseline 8. Subjects must possess a functional / usable pair of spectacles with which they can achieve 20/25 Snellen visual acuity or better at distance and near, and bring them to the visit 9. The subject's vertex corrected spherical distance refraction must be in the range (+/-0.25 D) of -2.00 D to -6.00 D (inclusive) in each eye 10. The subject's vertex corrected refractive cylinder must be equal or less than -0.75 diopters in each eye 11. Contact lens wearers must have spherical best corrected visual acuity of 20/25 or better in each eye. 12. Snellen visual acuity at distance and near must be within 1 line between subject's own spectacle and the manifest refraction, distance and near, OD & OS. Potential subjects who meet any of the following criteria will be excluded from participating in the study: Exclusion Criteria after Screening: 1. Currently pregnant or lactating, by self-report 2. Any ocular or systemic allergies, disease or use of

	medication which may interfere with contact lens wear and/or participation in the study (at the discretion of the investigator). 3. Any active ocular abnormalities/conditions that may interfere with contact lens wear and/or participation in the study (at the discretion of the investigator). 4. Any corneal distortion resulting from previous hard or rigid gas permeable contact lens wear 5. Habitual contact lens wear modality as extended wear (≥1 night per month of extended wear) 6. Habitual contact lens is rigid gas permeable, toric, monovision or multi-focal 7. Habitual spectacle contains an add power, photochromic or tint. 8. Any previous, or planned (during the course of the study) ocular surgery (e.g., radial keratotomy, PRK, LASIK, etc.) 9. Participation in any contact lens or lens care product clinical trial within 2 weeks prior to study enrollment. 10. Employee or employee's immediate family member of clinical site (e.g., Investigator, Coordinator, Technician) 11. Current habitual use of Restasis, Xiidra, ocular steroids, or any medication (RX or OTC) that may interfere with contact lens wear and/or participation in the study (at the discretion of the investigator) Exclusion Criteria after Baseline 12. Any ocular allergies, infections or other ocular abnormalities that are known to interfere with contact lens wear and/or participation in the study. This may include, but not be limited to entropion, ectropion, extrusions, chalazia, recurrent styes, glaucoma, history of recurrent corneal erosions, aphakia, or corneal distortion 13. Any Grade 3 or greater biomicroscopy findings (this includes, corneal edema, corneal staining, corneal vascularization, conjunctival injection, tarsal abnormalities, bulbar injection) on the FDA classification scale ([redacted]. 14. Accommodative/binocular dysfunction, determined by study procedures.
Disallowed Medications/Interventions	Restasis, Xiidra, ocular steroids, or any medication (Rx or OTC) that may interfere with contact lens wear or participation in the study at the discretion of the investigator

Measurements and Procedures	Ocular characteristics: non-invasive break up time (NIBUT)/ Non-invasive keratometric break up time (NIKBUT), Meibomian gland expressibility, blink patterns, conjunctival staining, and lid wiper epitheliopathy, Biomicroscopy [redacted] Snellen and logMAR Visual Acuity: Distance and Near Accommodative/binocular testing: Cover test, Global stereo, NRA/PRA Subjective symptomatology: Time point modified Dry Eye Questionnaire responses [redacted] subjective comfort rating using numeric scale via text responses, digital device use and the related ocular symptoms surveys
Microbiology or Other Laboratory Testing	None
Study Termination	The occurrence of one or more Unanticipated Adverse Device Effect (UADE), or any SAE where relationship to study agent cannot be ruled out, will result in stopping further dispensing investigational product. In the event of a UADE or SAE, the Sponsor Medical Monitor may unmask the treatment regimen of subject(s) and may discuss this with the Principal Investigator before any further subjects are enrolled.
Ancillary Supplies/ Study-Specific Materials (as applicable by site)	LogMAR visual acuity charts for distance and near Live view placedo disc corneal topographer (Medmont or like instrument) or Oculus Keratograph 5M Lipiview II Korb Meibomian Gland Evaluator (MGE) Sodium Fluorescein strips Lissamine Green strips Lacripure / ScleralFil
Principal Investigator(s) and Study Institution(s)/Site(s)	A full list of Principal Investigators, clinical sites, and institutions is kept separately from the Study Protocol and is included in the study Trial Master File.

Figure 1: Study Flowchart



COMMONLY USED ABBREVIATIONS AND DEFINITIONS OF TERMS

ADD	Plus Power Required For Near Use
ADE	Adverse Device Effect
AE	Adverse Event/Adverse Experience
BCVA	Best Corrected Visual Acuity
BSCVA	Best Spectacle Corrected Visual Acuity
CFR	Code of Federal Regulations
CLUE	Contact Lens User Experience
COAS	Complete Ophthalmic Analysis System
COM	Clinical Operations Manager
CRA	Clinical Research Associate
CRF	Case Report Form
CRO	Contract Research Organization
CT	Center Thickness
[redacted]	[redacted]
D	Diopter
DMC	Data Monitoring Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
ETDRS	Early Treatment Diabetic Retinopathy Study
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IDE	Investigational Device Exemption
IEC	Independent Ethics Committee
IRB	Institutional Review Board
ISO	International Organization for Standardization
ITT	Intent-to-Treat
JJVC	Johnson & Johnson Vision Care, Inc.
LC	Limbus Center
LogMAR	Logarithm of Minimal Angle of Resolution
MedDRA©	Medical Dictionary for Regulatory Activities
MOP	Manual of Procedures
NIBUT	Non-Invasive Break-Up Time
NIKBUT	Non-Invasive Keratography Break-Up Time
NIH	National Institutes of Health
NRA	Negative Relative Accommodation
OD	Right Eye
OHRP	Office for Human Research Protections
OHSR	Office for Human Subjects Research
OS	Left Eye
OU	Both Eyes
PD	Protocol Deviation

PHI	Protected Health Information
PI	Principal Investigator
PIG	Patient Instruction Guide
PQC	Product Quality Complaint
PRA	Positive Relative Accommodation
PRO	Patient Reported Outcome
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event/Serious Adverse Experience
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SD	Standard Deviation
SOP	Standard Operating Procedure
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect
VA	Visual Acuity

1. INTRODUCTION AND BACKGROUND

When exploring differences in characteristics between spectacle and contact lens wear during digital device use, controlled clinical studies provide information on objective and subjective endpoints. This study will enroll subjects in strata based on a Characterization Questionnaire to determine their time of, and symptomatology with typical digital device use. Evaluation of characteristics in physiology and symptomatology aim to guide learning into the ocular effects of digital device use in study lenses, and subject's own habitual contact lenses and spectacles. The scope of this study will focus on objective metrics found to be associated with lens comfort. Subjective comfort metrics will also be collected. Subjects with accommodative/binocular dysfunction will be excluded.

1.1. Name and Descriptions of Investigational Products

This study will use a single contact lens type: ACUVUE OASYS® 1-Day with HydraLuxe™ Technology, made of senofilcon A material, an FDA approved product. Further details about the test articles are found in Section 6 of this protocol.
The control will be the subject's own spectacle.

1.2. Intended Use of Investigational Products

The intended use of the investigative product is to compensate for ametropia.
During the study, subjects in the interventional arm will bilaterally wear the test lens in daily disposable modality for approximately 1 week.
All subjects will wear their own spectacle for approximately 1 week.

1.3. Summary of Findings from Nonclinical Studies

Not Applicable – Marketed product only

1.4. Summary of Known Risks and Benefits to Human Subjects

The following risks/adverse events can be associated with wearing soft contact lenses in general:
• The eyes may burn, sting and/or itch.
• There may be a feeling of something in the eye (foreign body, scratched area).
• There may be the potential for some temporary impairment due to peripheral infiltrates, peripheral corneal ulcers and corneal erosion.
• There may be the potential for other physiological observations, such as local or generalized edema, corneal neovascularization, corneal staining, injection, tarsal abnormalities, iritis and conjunctivitis, some of which are clinically acceptable in low amounts.
• There may be excessive watering, unusual eye secretions, or redness of the eye.
• Poor visual acuity, blurred vision, rainbows or halos around objects, photophobia, or dry eyes may also occur if the lenses are worn continuously or for too long a time.

There is no direct benefit to the subject for participating in the study, although they will be able to try marketed contact lenses.

For the most comprehensive clinical information regarding ACUVUE OASYS® 1-Day with HydraLuxe™ Technology (senofilcon A) contact lenses, refer to the latest version of the package insert.

1.5. Relevant Literature References and Prior Clinical Data Relevant to Proposed Clinical Study

For the most comprehensive clinical information regarding ACUVUE OASYS® 1-Day with HydraLuxe™ Technology (senofilcon A) contact lenses, refer to the latest version of the package insert (APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT).

2. STUDY OBJECTIVES, ENDPOINTS AND HYPOTHESES

2.1. Objectives

Primary Objective(s)
Compare between Test lens and Spectacles with respect to non-invasive break up time (NIBUT)/ non-invasive keratography break up time (NIKBUT) among habitual lens users.

Secondary Objective(s)
Compare between Test lens and Spectacles with respect to Meibomian gland expressibility, conjunctival staining, and lid wiper epitheliopathy among habitual lens users.

Other Objective(s)
Compare between Test lens and Spectacles among habitual lens users with respect to digital device_ocular symptoms, digital device use, blink characteristics, and subjective sensitivity.

The same comparisons presented above will be conducted between Spectacles/Test lens for habitual lens users and Spectacles for habitual spectacle users.

2.2. Endpoints

Primary Endpoint(s)

Non-invasive break up time (NIBUT)/ non-invasive keratography break up time (NIKBUT) time in seconds

NIBUT/NIKBUT is measured as the time interval in seconds after the final blink to the first appearance of distortion in the reflected rings; or to the time that the participant has to blink due to discomfort.

Secondary Endpoint(s)

Meibomian Gland Expressibility (Appendix I)

Meibomian gland expressiblity is assessed in three regions of the lower eyelid: temporal, central, and nasal. Approximately five glands are expressed per region and evaluated using a four-grade scale: 0 = No Secretion, 1 = Inspissated, 2 = Colored/Cloudy Liquid, and 3 = Clear Liquid Oil. The total score is calculated as the sum of all grades across the three regions and ranges from 0 to 45.

Conjunctival Staining [redacted]

Conjunctival staining is graded and recorded by quadrant (Superior, Inferior, Nasal, and Temporal) using the following grading scale: Grade 0 = None, Grade 1 = Trace, Grade 2 = Mild, Grade 3 = Moderate, and Grade 4 = Severe. Average grade can be calculated based on grades of the four quadrants.

Lid Wiper Epitheliopathy (Appendix H)

Horizontal lid margin staining and sagittal lid margin staining are graded for each eyelid separately. The horizontal and sagittal grades are then averaged for each eyelid to obtain the upper lid average grade and lower lid average grade. The final grade is the average of the upper and lower lid average grades. Subjects can be classified according to their final grades for each eye. The classification is defined as follows: “None” for final grades of 0, “Mild” for final grades between 0.25 and 1.00, “Moderate” for final grades between 1.25 and 2.00, and “Severe” for final graded between 2.25 and 3.00.

Other Exploratory Endpoint(s)

Subjective Comfort Assessed by (0-100) Numeric Scale

Subjective comfort will be assessed using a numeric scale which ranges from 0 to 100, where 100 is defined as “Best comfort imaginable” and 0 as “Worst comfort imaginable”.

Dry Eye Symptoms Measured by CLDEQ-8 and/or DEQ-5 [redacted]

Subject dry eye symptoms will be evaluated using the Contact Lens Dry Eye Questionnaire-8 (CLDEQ-8). The CLDEQ-8 is a validated outcome measure for soft contact lenses wearers. It has been highly correlated with habitual baseline status and change in overall opinion when subjects are refit with contact lenses. The sum of the item scores of CLDEQ-8, ranging from 0 to 37, will be used to assess dry eye symptoms, where higher scores indicate more serious symptoms.

Digital Device Ocular Symptoms
Ocular symptoms related to digital device use will be assessed using the digital device ocular symptoms questionnaire and MRD items. The digital device ocular symptoms questionnaire was modified based on CLDEQ-8. The sum of item scores range from 0 to 37.

Digital Device Use
Digital device use will be examined using MRD items.

Subjective sensitivity measured by Highly Sensitive Person-HSP Scale
Subjective sensitivity will be assessed using the Highly Sensitive Person – HSP scale. The HSP scale consists of 27 items on the 7-point Likert scale (1 for "Not at all" and 7 for "Extremely"). Mean score across the 27 items will be calculated.

Blink characteristics
Blink characteristics include blink patterns, total number of blinks, and percent of partial blinks over a 20 second measurement duration.

2.3. Hypotheses

This is a pilot study and all the hypotheses are exploratory in nature.

Primary Hypotheses

There will be no difference between Test lens and Spectacles with respect to non-invasive break up time/ non-invasive keratography break up time among habitual contact lens wearers (the interventional arm) at 1-Week follow-up.

Secondary Hypotheses

There will be no secondary hypotheses. The following will be estimated for Test lens and Spectacles among habitual contact lens wearers at 1-Week follow-up:

- Total scores of Meibomian gland expressibility
- Average grades of conjunctival staining
- Proportions of eyes with clinically significant (Grade 3 or 4 of overall classification) lid wiper epitheliopathy

3. TARGETED STUDY POPULATION

3.1. General Characteristics

Subjects, ages 18-42 are to complete this clinical study. Subjects will be stratified into two arms: 20 that are full time spectacle wearers (observational arm), and 40 subjects that are current spherical soft contact lens wearers (interventional arm). Within each arm, half of subjects will have been classified as symptomatic high digital device users.

3.2. Inclusion Criteria

Potential subjects must satisfy all of the following criteria to be enrolled in the study:

Inclusion Criteria after Screening

1. The subject will have completed the pre-screening Classification questionnaire.
2. Subject must have a working cell phone capable of sending and receiving text messages.
3. The subject must read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form.
4. Appear able and willing to adhere to the instructions set forth in this clinical protocol
5. Between 18 and 42 (inclusive) years of age at the time of screening
6. Be a current soft contact lens wearer in both eyes with a minimum of 5 days/week wear time over the last 1 month by self-report OR be a full time spectacle wearer (7 days/ week) without contact lens wear over the last 6 months
7. Subjects must be willing to adhere to spectacle-only refractive correction for approximately 1 week

Inclusion Criteria after Baseline

8. Subjects must possess a functional / usable pair of spectacles with which they can achieve 20/25 Snellen visual acuity or better at distance and near, and bring them to the visit
9. The subject's vertex corrected spherical distance refraction must be in the range (+/-0.25 D) of -2.00 D to -6.00 D (inclusive) in each eye
10. The subject's vertex corrected refractive cylinder must be equal or less than -0.75 diopters in each eye
11. Contact lens wearers must have spherical best corrected visual acuity of 20/25 or better in each eye.
12. Snellen visual acuity at distance and near must be within 1 line between subject's own spectacle and the manifest refraction, distance and near, OD & OS.

3.3. Exclusion Criteria

Potential subjects who meet any of the following criteria will be excluded from participating in the study:

Exclusion Criteria after Screening:

1. Currently pregnant or lactating, by self-report
2. Any ocular or systemic allergies, disease or use of medication which may interfere with contact lens wear and/or participation in the study (at the discretion of the investigator).
3. Any active ocular abnormalities/conditions that may interfere with contact lens wear and/or participation in the study (at the discretion of the investigator).
4. Any corneal distortion resulting from previous hard or rigid gas permeable contact lens wear

5. Habitual contact lens wear modality as extended wear (≥1 night per month of extended wear)
6. Habitual contact lens is rigid gas permeable, toric, monovision or multi-focal
7. Habitual spectacle contains an add power, photochromic or tint.
8. Any previous, or planned (during the course of the study) ocular surgery (e.g., radial keratotomy, PRK, LASIK, etc.)
9. Participation in any contact lens or lens care product clinical trial within 2 weeks prior to study enrollment.
10. Employee or employee's immediate family member of clinical site (e.g., Investigator, Coordinator, Technician)
11. Current habitual use of Restasis, Xiidra, ocular steroids, or any medication (RX or OTC) that may interfere with contact lens wear and/or participation in the study (at the discretion of the investigator)

Exclusion Criteria after Baseline

12. Any ocular allergies, infections or other ocular abnormalities that are known to interfere with contact lens wear and/or participation in the study. This may include, but not be limited to entropion, ectropion, extrusions, chalazia, recurrent styes, glaucoma, history of recurrent corneal erosions, aphakia, or corneal distortion
13. Any Grade 3 or greater biomicroscopy findings (this includes, corneal edema, corneal staining, corneal vascularization, conjunctival injection, tarsal abnormalities, bulbar injection) on the FDA classification scale [redacted]
14. Accommodative/binocular dysfunction, determined by study procedures.

3.4. Enrollment Strategy

Study subjects will be recruited from the Institution/clinical site's subject database and/or utilizing Independent Ethics Committee (IEC) or Institutional Review Board (IRB) approved materials.
The clinical site will administer a pre-screening on potential subjects before they attend the initial study visit utilizing IEC/IRB approved recruitment materials.

4. STUDY DESIGN AND RATIONALE

4.1. Description of Study Design

This is two-arm study. There will be an observational arm and an interventional arm.

In the observational arm, habitual spectacle wearers will all continue to use their habitual optical correction and undergo ocular evaluations and questionnaires at 2 separate study visits: baseline and 1-week. Since the nature of this arm is observational, it will be non-controlled, non-randomized, and unmasked.

In the interventional arm, habitual contact lens wearers who own spectacles will undergo a bilateral, 1-week dispensing, randomized, controlled, unmasked, 2×2 cross-over study with a 1-week washout between periods in which subjects will wear their habitual contact lens.

Each subject will be bilaterally fitted with the one test article and crossed with their own spectacle in 2 periods.

4.2. Study Design Rationale

To investigate the difference in ocular characteristics between contact lens wear and spectacle wear among habitual contact lens wearers, a 2-treatment by 2-period cross-over design (Spectacle / ACUVUE OASYS 1-Day or ACUVUE OASYS 1-Day /Spectacle) will be used with a 1-week washout between the two study periods to eliminate any potential carryover effect. Cross-over design is employed because, if the no-carryover assumption is met, treatment differences are measured within a subject rather than between subjects which makes a more precise measurement. In addition to the interventional arm of habitual contact lens wearers, an observational arm will be added to investigate ocular characteristics among habitual spectacle wearers which serves as a reference group.

4.3. Enrollment Target and Study Duration

The target is to enroll approximately 70 eligible subjects with 60 subjects to complete the study. Subjects will be stratified into two arms: 20 subjects that are full time spectacle wearers (observational arm), and 40 subjects that are current spherical soft contact lens wearers (interventional arm). Within each arm, subjects will be dichotomized into two groups via the Classification Questionnaire. Group 1: half of subjects will have been classified as symptomatic high digital device users. Group 2: half of subjects will be classified as having low digital device use and/or asymptomatic with digital device use

The table below provides details of subject enrollment.

Table 1: Subject Enrollment

	Habitual Spectacle Wearers (observational arm)		Habitual Contact Lens Wearers (interventional arm)		Total
	Group 1: High use and Symptomatic	Group 2: Low use and/or Asymptomatic	Group 1: High use and Symptomatic	Group 2: Low use and/or Asymptomatic	
Randomized (as applicable)	12	12	23	23	70
Complete	10	10	20	20	60

There will be 2 visits for the observational arm and 4 visits for the interventional arm. The study is anticipated to last 6 weeks and include a 2-week enrollment period.

5. TEST ARTICLE ALLOCATION AND MASKING

5.1. Test Article Allocation

Dispensed contact lenses will be worn in a bilateral fashion. Randomization is applicable in this study only in the interventional arm. Study lens and Spectacle will be worn in a bilateral

and random fashion for a period of 1 week each among subjects in the interventional arm. Subjects will be randomly assigned to one of two sequences (Spectacle /ACUVUE OASYS 1-Day or ACUVUE OASYS 1-Day /Spectacle). Groups based on the Classification questionnaire will be used as strata in the randomization, with a 1: 1 ratio for Group 1 (high use and symptomatic) and Group 2 (low use and/or asymptomatic) subjects.

The test article assignment of subjects must be performed at the Initial Visit. The following must have occurred prior to test article assignment:
- Informed consent has been obtained
- Subject meets all the applicable inclusion/exclusion criteria
- Subject history and baseline information has been collected

5.2. Masking

This study is not masked, since it is evident whether the subject is using spectacles or contact lenses; subjects and investigators will be aware of the test article assignment (Test lens/Spectacles). However, the brand name of the Test lens will be masked to subjects through over labeling to reduce any potential bias with brand name preference on subjective assessment of comfort, dry eye symptoms, and sensitivity testing.

5.3. Procedures for Maintaining and Breaking the Masking

Not applicable since this study is not masked.

6. STUDY INTERVENTION

6.1. Identity of Test Articles

The control will be the subject's own spectacle.

The following contact lens will be used in this study:

Table 2: Test Lens

	Test 1
Name	ACUVUE OASYS®1-Day with HydraLuxe™ Technology
Manufacturer	JJVC
[redacted]	[redacted]
Lens Material	Senofilcon A
Nominal Base Curve @ 22 °C	8.5
Nominal Diameter @ 22 °C	14.3
Nominal Distance Powers (D)	-2.00 to -6.00 (0.25 steps)
Nominal Cylinder Powers (D) and Axes	N/A
Nominal ADD Powers (D)	N/A
Center Thickness (Optional)	0.085
Oxygen Permeability (Dk)	103.0

	Test 1
Wear Schedule in Current Study	Daily Disposable
Replacement Frequency	Daily
Packaging Form (vial, blister, etc.)	Blister
Other distinguishing items (e.g., dye, packaging solution, optical design, etc.)	JJVC marketed and FDA approved production lenses

In this study, each of 40 subjects will be fit bilaterally in daily disposably modality for up to 8 days (40 × 2 × 8). Approximately 640 contact lenses will be used in this study.

6.2. Ancillary Supplies/Products

The following supplies and equipment will be used in this study:

Table 3: Ancillary Supplies/Equipment

Supplies				
Supply Name/ Description	ScleralFil/ Ophthalmic Saline	Lacripure/ Ophthalmic Saline	GREENGLO/ Lissamine Green dye strips	Fluorescein dye strips
Manufacturer	Bausch & Lomb	Menicon	HUB Pharmaceuticals	N/A
Preservative	None	None	None	None
Indication	Unit dose; Sterile, buffered isotonic (0.9%NaCl) saline solution	Unit dose; Sterile, normal (0.9%NaCl) saline solution	Diagnostic	Diagnostic
Equipment				
Equipment Name/ Description	LipiView	Corneal Topographer	Meibomian Gland Evaluator	LogMAR Visual Acuity Charts
Manufacturer	TearScience	OCULUS, Inc.; Medmont, or like instrument	JJV	Precision Vision

Supplies				
Diagnostic	Blink patterns	Non invasive keratography tear break up time / Non invasive break up time	Meibomian Gland Expressibility	HLHC Distance (charts HC1, HC2) and near Retinopathy Study (ETDRS) 2000 Series (charts 1, 2)

6.3. Administration of Test Articles

Test articles will be dispensed to subject meeting all eligibility requirements, including any dispensing requirements set forth in this clinical protocol. Subjects will be dispensed an adequate supply of test articles to complete the study. Lost or damaged test articles may be replaced at the discretion of the Investigator and/or the Sponsor.

6.4. Packaging and Labeling

The test articles will be packaged in blisters as the primary packaging. The test article will be over-labeled to mask the subject to the identity of the lens. The test articles will be in investigational cartons sealed with a tamper evident seal or in plastic bags as the secondary packaging form. The sample study label is shown below:

6.5. Storage Conditions

Test articles will be maintained at ambient temperatures at the clinical site. Test articles must be kept under secure conditions.

6.6. Collection and Storage of Samples

Ex-vivo (worn) lenses collected at VRC will be retained dry in vials and frozen in the clinic's freezer, to be collected periodically throughout the study by the sponsor.

Ex-vivo (worn) lenses from other clinical study site(s) will be discarded, unless associated with an Adverse Event and/or Product Quality Complaint.
When possible, any lens or test article associated with an Adverse Events and/or a Product Quality Complaint must be retained and stored in a glass vial with moderate solution pending directions from the sponsor for potential return back to JJVC.

6.7. Accountability of Test Articles

JJVC will provide the Investigator with sufficient quantities of study articles and supplies to complete the investigation. The Investigator is asked to retain all lens shipment documentation for the test article accountability records.

Test article must be kept in a locked storage cabinet, accessible only to those assigned by the Investigator for dispensing. The Investigator may delegate this activity to authorized study site personnel listed on the Site Delegation Log. All test articles must be accounted. This includes:

1. What was dispensed for the subject for trial fitting, to wear out of the office, or issued for the subject to replace appropriately between visits
2. What was returned to the Investigator unused
3. The number and reason for unplanned replacements

The Investigator will collect all unused test articles from the subjects at the end of the subject's participation. Subject returned unused test articles must be separated from the clinical study inventory of un-dispensed test articles, and must be labeled with the subject number and date of return. Following final reconciliation of test articles by the monitor, the Investigator or monitor will return all unused test articles to JJVC.

If there is a discrepancy between the shipment documents and the contents, contact the study monitor immediately.

Reference [redacted] Site Instructions for Test Article Receipt and Test Article Accountability for additional information.

7. STUDY EVALUATIONS

7.1. Time and Event Schedule

Table 4: Time and Events

Visit Information	Visit 1 Screening, Baseline, Treatment 1	Visit 2 Treatment 1 Follow-up	Washout (5-7 days)	Visit 3 Treatment 2	Visit 4 Treatment 2 Follow-up, Final Evaluation
Time Point	Day 1	6-8 days after Visit 1		6-8 days after Visit 2	6-8 days after Visit 3

Estimated Visit Duration	2.5 hours	1.5 hours	[redacted]	1.5 hours	1.5 hours
Statement of Informed Consent	x				
Demographics	x				
Medical History/Concomitant Medications	x	x		x	x
Habitual Contact Lens/Spectacles Information	x				x
Inclusion/Exclusion Criteria	x				
Baseline Questionnaires	x				
Subject Stratification	x				
Entrance Visual Acuity	x	x			x
Habitual Lens/Spectacle Testing (if applicable)	x			x	
Keratometry	x				
Subjective Sphero-Cylindrical Refraction	x				
Subjective Best Sphere Refraction	x			x	
NRA/PRA	x				
Slit Lamp Biomicroscopy	x	x		x	x
Spectacle corrected Visual Acuity	x				
Eligibility after Baseline	x				
Lens Selection	x			x	
Lens Insertion & Settling	x			x	
Visual Acuity and Over Refraction		x		x	
Lens Power Modification (if applicable)					
Subject Reported Ocular Symptoms	x	x		x	
Post Fit Questionnaires				x	
Lens Fit Assessment	x	x			x
Distance ETDRS LogMAR Visual					

Visit Information	Visit 1 Screening, Baseline, Treatment 1	Visit 2 Treatment 1 Follow-up	Washout (5-7 days)	Visit 3 Treatment 2	Visit 4 Treatment 2 Follow-up, Final Evaluation
Time Point	Day 1	6-8 days after Visit 1		6-8 days after Visit 2	6-8 days after Visit 3
Estimated Visit Duration	2.5 hours	1.5 hours		1.5 hours	1.5 hours
Acuity					
Wettability		x		x	x
Surface Debris & Deposits		x		x	x
Tear film testing		x		x	x
Blink patterns		x			x
Lid wiper epitheliopathy		x			x
Conjunctival staining		x		x	x
Meibomian Gland Expressibility		x			
Exit Snellen Distance Visual Acuity	x	x		x	
Dispense Patient Instruction Guide	x				
Dispense Test Article	x			x	
Lens wear time	x	x			x
SMS text message set up	x				
Follow-up Questionnaire		x			x
Study Completion					x

7.2. Detailed Study Procedures

Pre-Visit Screening: If applicable
(via phone or email)

PRE- VISIT COMMUNICATION		
Step	Procedure	Details
0.1	Preliminary Subject Identification	The clinical study site will search through their subject database to find potential subjects who may be eligible to participate. Subjects may be contacted by telephone or sent an electronic survey via email.
0.2	Subject's Privacy Notice and Disclosure	The clinical study site must provide notice to subjects regarding the collection and disclosure of personal information. Each subject must provide verbal consent by phone to allow the collection and disclosure of the

		personal information collected in the screening questionnaire. The verbal consent will be documented in the Screening Questionnaire.
0.3	Pre-screening Classification Questionnaire	Subject will be contacted by the clinical study site to complete a pre-screening questionnaire (which will be provided separately) over the phone or via email to determine preliminary eligibility.

VISIT 1

Subjects must present to Visit 1 wearing their habitual correction for at least 6 hours. Habitual spectacle wearers will present with spectacles; habitual contact lens wearers will present with contact lenses on eye and spectacles in hand.

Visit 1: Screening			
Step	Procedure	Details	[redacted]
1.1	Statement of Informed Consent	Each subject must read, understand, and sign the Statement of Informed Consent before being enrolled into the study. The Principal Investigator or his/her designee conducting the informed consent discussion must also sign the consent form. **Note**: The subject must be provided a signed copy of this document.	
1.2	Demographics	Record the subject's year of birth, gender, race and ethnicity.	
1.3	Medical History and Concomitant Medications	Questions regarding the subjects' medical history and concomitant medications.	
1.4	Habitual Spectacles	Record the subject's habitual spectacle: lensometry, wear time, age of Rx. Subjects whose spectacles incorporate an add, tint or photochromic will be discontinued.	
1.5	Habitual Lenses (if applicable)	Questions regarding the subject's habitual lens type and parameters.	
1.6	Current contact lens wear times (if applicable)	Record the mode of their current contact lens wear, as well as their habitual wear time (WT) and comfortable wear time (CWT).	
1.7	Classification Questionnaire	The subject will respond to a Questionnaire to classify them by group (Appendix A)	
1.8	Eligibility after Screening	All responses to Screening Inclusion Criteria questions must be answered "yes" and all responses to Exclusion Criteria must be answered "no" for the subject to be considered eligible.	

Visit 1: Screening			
Step	Procedure	Details	[redacted]
		If subject is deemed to be ineligible after screening, proceed to Final Evaluation and complete Subject Disposition. Refraction and Biomicroscopy forms are not required.	
1.9	Subject Stratification	Subjects who are habitual spectacle wearers will be assigned to the observational arm. Subjects who are habitual contact lens wearers will be assigned to the interventional arm. Subjects not needed to fulfill classification enrollment targets may be discontinued.	
1.10	Subject Classification	Subjects will be dichotomized by their Classification Questionnaire.	

Visit 1: Baseline			
Step	Procedure	Details	[redacted]
1.11	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]
1.12	Baseline Spectacle questionnaires (if applicable): DEQ-5, MRD, and Digital Device	The subject will respond to the Baseline Spectacle Questionnaires.	[redacted]
1.13	Baseline Contact lens Questionnaires (if applicable): CLDEQ-8, MRD, and Digital Device	The subject will respond to the Contact Lens Questionnaire.	[redacted]
1.14	Entrance Visual Acuity	Record the distance and near LogMAR visual acuity (OD, OS) to the nearest letter.	[redacted]
1.15	Habitual Lens Subjective Lens Fit Assessment (if applicable)	Evaluate overall lens fit acceptance (acceptable or unacceptable) based on centration, movement and other fitting characteristics. An unacceptable fit is deemed by one of the following criteria: • limbal exposure at primary gaze or with extreme eye movement; • edge lift; excessive movement in primary and up gaze; or insufficient movement in all three of the following conditions: primary gaze, up gaze, and Josephson push up.	[redacted]

Visit 1: Baseline			
Step	Procedure	Details	[redacted]
		Note: ***if lens fit is unacceptable subject will be discontinued from the study.***	
1.16	Cover test	Perform unilateral cover test with correction, distance and near to rule out strabismus	
1.17	Global Stereo	Perform global stereo testing at near to confirm binocularity. Using polarized glasses and a Randot SO-002 Stereoptical Book (or similar), presence of random-dot stereopsis at 250 second of arc will be tested with correction.	
1.18	Lens Removal and Storage (if applicable)	If present, the lenses will be removed by the subject and stored in appropriate solution or discarded if appropriate.	[redacted]
1.19	Spectacle corrected visual acuity (if applicable)	For subjects that have just removed their contact lens: Record the distance and near LogMAR visual acuity (OD, OS) to the nearest letter.	[redacted]
1.20	Keratometry	Record the keratometry readings OD and OS in diopters.	[redacted]
1.21	Subjective Best Sphere Refraction (if interventional arm)	Complete subjective Best Sphere refraction and record the resultant Snellen distance visual acuity (OD, OS) to the nearest letter.	[redacted]
1.22	Subjective Sphero-cylindrical Refraction	Complete subjective spherocylindrical refraction and record the Snellen resultant distance and near visual acuity (OD, OS) to the nearest letter. Near (40 centimeters): • Early Treatment Diabetic Retinopathy Study (ETDRS) 2000 Series (charts 1, 2).	[redacted]
1.23	Negative relative accommodation / Positive relative accommodation (NRA/PRA)	Perform NRA/PRA in phoropter. NRA should be +1.75D to +3.00D (inclusive). PRA should be ≤ -1.75D. If found to be outside of these values, the subject will be discontinued at this time.	[redacted]
1.24	Slit Lamp Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility. If any of these slit lamp findings are grade 3 or higher, the subject may not continue at this time, but may return up to one additional time	[redacted]

Visit 1: Baseline			
Step	Procedure	Details	[redacted]
		to determine eligibility at the investigator's discretion. If discontinued a final examination must be completed.	
1.25	Eye Rinse	If the clearance if dye needs to be expedited, the study investigator or technician will rinse the subject's eyes thoroughly with a study provided solution.	
1.26	Spectacle corrected Visual Acuity	Record the distance and near Snellen visual acuity (OD, OS) to the nearest letter. Subjects must read the smallest line until at least 50% of the letters are read incorrectly. Near (40 centimeters): • Early Treatment Diabetic Retinopathy Study (ETDRS) 2000 Series (charts 1, 2). Snellen visual acuity at distance and near must be within 1 line between subject's own spectacle and the manifest refraction, distance and near, OD & OS to continue.	[redacted]
1.27	Eligibility after Baseline	All responses to Inclusion Criteria questions must be answered "yes" and all responses to Exclusion Criteria questions must be answered "no" for the subject to be considered eligible. If a subject is deemed to be ineligible after baseline, proceed to Final Evaluation and complete all forms.	
1.28	Randomization (if applicable)	If a subject is enrolled into the interventional arm, they will be randomized per the randomization scheme.	
1.29	Treatment Selection (if applicable)	Assign the treatment based on the randomization scheme. Subjects assigned spectacle wear will continue to step 1.30. Subjects assigned contact lens wear will continue to Step 1.32	
1.30	SMS text message set up	Text message program will be set up and subject will be instructed on use. They will provide the average time they stop using their glasses/contact lenses each evening and the text message will be set to be sent 30 minutes prior to that time.	
1.31	Subject instruction	The subjects will be scheduled for Visit 2 in	

Visit 1: Baseline			
Step	Procedure	Details	[redacted]
		6-8 days and will present after at least 6 hours of spectacle wear on the day of the visit.	

Visit 1: Treatment 1 (Study lens fitting)			
Step	Procedure	Details	[redacted]
1.32	Lens Insertion	Select the contact lens power based on subjective best sphere refraction. The subject inserts the study lenses. Record the time of lens insertion. Check for lens damage under the slit lamp before proceeding with lens settling. Replace damaged lenses if applicable.	
1.33	Lens Settling	Allow the study lenses to settle for a minimum of 5 minutes.	
1.34	Subjective Best Sphere Over Refraction	Perform subjective best sphere refraction over the study lenses and record the best corrected Snellen distance visual acuity to the nearest letter (OD, OS).	[redacted]
1.35	Lens Power Modification	Adjust the lens power if the subject's best sphere over-refraction is not plano. For each power modification, repeat steps (1.32-1.34). Up to one power modification is allowed.	
1.36	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]
1.37	Subjective Lens Fit Assessment	Evaluate overall lens fit acceptance (acceptable or unacceptable) based on centration, movement and other fitting characteristics. An unacceptable fit is deemed by one of the following criteria: • limbal exposure at primary gaze or with extreme eye movement • edge lift • excessive movement in primary and up gaze • insufficient movement in all three of the following conditions: primary gaze, up gaze, and Josephson push up **Note**: ***if lens fit is unacceptable subject will be discontinued from the study.***	[redacted]

Visit 1: Treatment 1 (Study lens fitting)			
Step	Procedure	Details	[redacted]
1.38	Contact Lens corrected Visual Acuity	Perform monocular distance and near ETDRS LogMAR visual acuity test, OD & OS	[redacted]
1.39	Exit Snellen Visual Acuity	Record the Snellen visual acuity, distance and near, OD & OS. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.	[redacted]
1.40	Continuance	For the subject to continue in the study, they must meet all three of the following criteria: • Snellen visual acuity is 20/25 or better, distance and near (OD, OS) • The lens fit is acceptable OD and OS • Investigator approval If the Investigator does not approve the dispensing of the first study lens, then the study is terminated for that subject.	
1.41	Dispense	The lenses will be dispensed for a 6-8 day wearing period. During this time, they are required to wear the lenses at least 5 days and at least 8 hours per day that they are worn. • Dispense enough lenses to last the subject to their scheduled follow-up visit. Do not dispense extras* • The lenses will be worn as daily wear/daily disposable only • A patient instruction booklet will be provided • Subjects will be scheduled for their 1-week follow-up visit, ensuring that they wear the study lens at least 6 hours on the day of the follow-up visit * **Note:** In the event a lens is lost or damaged, the subject will return to the clinical site for replacement. As much as reasonably possible, a damaged lens and packaging should be returned to the clinical site (wet, if possible) and then returned to the Sponsor. If lens damage is present, complete the Product Quality Complaint Form. The lens will be stored in labeled vial with saline, and clearly differentiated from the other worn lenses that will be shipped back to the Sponsor.	

Visit 1: Treatment 1 (Study lens fitting)			
Step	Procedure	Details	[redacted]
1.42	SMS text message set up	Text message program will be set up and subject will be instructed on use. They will provide the average time they stop using their glasses/contact lenses each evening and the text message will be set to be sent 30 minutes prior to that time.	
1.43	Subject instruction	The subjects will be scheduled for Visit 2 in 6-8 days and will present after at least 6 hours of contact lens wear time on the day of the visit. Advise subject to bring habitual contact lens or spectacles to their next visit.	

VISIT 2

The subjects must present to Visit 2, 6-8 days following Visit 1, after at least 6 hours of spectacle or contact lens wear time (as assigned) on the day of the visit.

Visit 2: Treatment 1 Follow-Up 1			
Step	Procedure	Details	[redacted]
2.1.	Adverse Events and Concomitant Medications Review	Review any changes to the subject's medical history or concomitant medications from the previous study visit. Record any changes, and any adverse events.	
2.2.	Wearing Time (if applicable)	Record the average wearing time and comfortable wearing time.	
2.3.	Compliance	Confirm compliance with the prescribed wear schedule.	
2.4.	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]
2.5.	Follow-Up Spectacle Questionnaires (if applicable): DEQ-5, MRD, and Digital Device	The subject will respond to the Follow-Up Questionnaire.	[redacted]
2.6.	Follow-Up Contact lens Questionnaires (if applicable): CLDEQ-8, MRD, and Digital Device	The subject will respond to the Follow-Up Questionnaire.	[redacted]
2.7.	Visual Acuity	Perform monocular distance and near ETDRS LogMAR visual acuity test, OD & OS	[redacted]
2.8.	Subjective Lens Fit	Evaluate overall lens fit acceptance	[redacted]

Visit 2: Treatment 1 Follow-Up 1			
Step	Procedure	Details	[redacted]
	Assessment (if applicable)	(acceptable or unacceptable) based on centration, movement and other fitting characteristics. An unacceptable fit is deemed by one of the following criteria: • limbal exposure at primary gaze or with extreme eye movement • edge lift • excessive movement in primary and up gaze • insufficient movement in all three of the following conditions: primary gaze, up gaze, and Josephson push up **Note**: ***if lens fit is unacceptable subject will be discontinued from the study.***	
2.9.	Wettability Characteristics (if applicable)	Record the white light lens wettability of both lenses.	[redacted]
2.10.	Surface Debris & Deposits (if applicable)	Record any front and back surface lens debris & deposits.	[redacted]
2.11.	Tear film stability (Pre-Lens or Pre-Corneal as applicable)	Record the first tear film stability (NIBUT/NIKBUT), OD & OS. Record three measurements.	(Appendix E & F)
2.12.	Blink patterns (as site applicable)	Record the Blink Patterns, OD & OS	Lipiview II manufacturer instructions (Appendix G)
2.13.	Pre-corneal or Pre-lens (as applicable) tear film lipid layer thickness as available by site	Record the tear film lipid layer thickness, OD & OS	Lipiview II manufacturer instructions (Appendix G)
2.14.	Lens Removal and Storage (if applicable)	The lenses will be removed by the subject. VRC site only, both lenses will be stored dry in a labeled glass vial and frozen, using study specific labels. Otherwise, lenses will be discarded.	[redacted]
2.15.	Slit Lamp Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility.	[redacted]

Visit 2: Treatment 1 Follow-Up 1			
Step	Procedure	Details	[redacted]
		If the subject has a Grade 3 slit lamp finding, it will be recorded as an Adverse Event	
2.16.	Lid wiper Epitheliopathy	Record the lid wiper epitheliopathy (upper & lower) by Lissamine green, OD & OS	Lid Wiper Epitheliopathy Work Aid (Appendix H)
2.17.	Conjunctival staining	Record the conjunctival staining by Lissamine green, OD & OS	[redacted]
2.18.	Meibomian Gland Expressibility (Lower lid, 3 regions)	Record the Meibomian Gland Expressibility, OD & OS via Meibomian Gland Secretion Grading Scale (Appendix I)	Procedure per Meibomian Gland Evaluator manufacturer instructions. (Appendix I)
2.19.	Eye Rinse	If the clearance if dye needs to be expedited, the study investigator or technician will rinse the subject's eyes thoroughly with a study provided solution.	
2.20.	Exit Visual Acuity (if applicable)	Record the Snellen distance visual acuity, OD & OS with habitual contact lenses or spectacles. Subjects must read the smallest line until at least 50% of the letters are read incorrectly. Record correction used.	[redacted]
2.21.	Subject Instruction	Subjects in the observational arm will complete the Exit Evaluation. Subject in the interventional arm will continue in the study: • Subjects in the interventional arm will be scheduled for Visit 3 following a one-week washout period in which they will wear their habitual lens per their habitual wear schedule, ensuring that they wear their habitual lens at **least 6 hours on the day of the next visit.**	

WASHOUT (5-7 days): One-week washout period in which subjects will wear their habitual lens per their habitual wear schedule

VISIT 3

The subjects must present to Visit 3, 6-8 days following Visit 2. The subjects must present after at least 6 hours of habitual contact lens wear time on the day of the visit.

Visit 3: Treatment 2			
Step	Procedure	Details	[redacted]
3.1.	Adverse Events and Concomitant Medications Review	Review any changes to the subject's medical history or concomitant medications from the previous study visit. Record any changes, and any adverse events.	
3.2.	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]
3.3.	Visual Acuity	Record the distance Snellen distance visual acuity with the contact lenses (OD, OS) to the nearest letter. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.	[redacted]
3.4.	Habitual lens Pre-Lens Tear film stability as available by site	Record the first tear film stability (NIBUT/NIKBUT), OD & OS. Record three measurements.	(Appendix E & F)
3.5.	Habitual lens Wettability Characteristics	Record the white light lens wettability of both lenses.	[redacted]
3.6.	Habitual Lens Surface Debris & Deposits	Record any front and back surface lens debris and deposits.	[redacted]
3.7.	Lens Removal and Storage	If present, the lenses will be removed by the subject and stored in appropriate solution or discarded if appropriate.	[redacted]
3.8.	Slit Lamp Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility. If the subject has a Grade 3 slit lamp finding, it will be recorded as an Adverse Event	[redacted]
3.9.	Lid wiper Epitheliopathy	Record the lid wiper epitheliopathy (upper & lower) by Lissamine green, OD & OS	Lid Wiper Epitheliopathy Work Aid (Appendix H)
3.10.	Conjunctival staining	Record the conjunctival staining by Lissamine green, OD & OS	[redacted]
3.11.	Eye Rinse	If the clearance if dye needs to be expedited, the study investigator or technician will rinse the subject's eyes thoroughly with a study provided solution.	

Visit 3: Treatment 2			
Step	Procedure	Details	[redacted]
3.12.	Continuance	Confirm subject eligibility	
3.13.	Treatment Selection	Assign the treatment based on the randomization scheme. Select the contact lens power based on subjective best sphere refraction.	
3.14.	Spectacle corrected Exit Visual Acuity	For Subjects wearing spectacles record the distance Snellen visual acuity (OD, OS) to the nearest letter. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.	[redacted]
3.15.	Spectacle corrected Subject instruction	The spectacle corrected subjects will be scheduled for Visit 4 in 6-8 days and will present after at least 6 hours of spectacle on the day of the visit. Subjects instructed to continue to participate in the SMS text messaging questionnaire.	
3.16.	Lens Insertion (if applicable)	The subject inserts the study lenses. Record the time of lens insertion. Check for lens damage under the slit lamp before proceeding with lens settling. Replace damaged lenses if applicable.	
3.17.	Lens Settling (if applicable)	Allow the study lenses to settle for a minimum of 5 minutes.	
3.18.	Subjective Best Sphere Over Refraction (if applicable)	Perform subjective best sphere refraction over the study lenses and record the best corrected distance Snellen visual acuity to the nearest letter (OD, OS).	[redacted]
3.19.	Lens Power Modification (if applicable)	Adjust the lens power if the subject's best sphere over-refraction is not plano. For each power modification, repeat steps (3.16-3.18). Up to one power modifications are allowed.	
3.20.	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]
3.21.	Subjective Lens Fit Assessment (if applicable)	Evaluate overall lens fit acceptance (acceptable or unacceptable) based on centration, movement and other fitting characteristics. An unacceptable fit is deemed by one of the following criteria: • limbal exposure at primary gaze or with extreme eye movement	[redacted]

Visit 3: Treatment 2			
Step	Procedure	Details	[redacted]
		• edge lift • excessive movement in primary and up gaze • insufficient movement in all three of the following conditions: primary gaze, up gaze, and Josephson push up **Note**: ***if lens fit is unacceptable subject will be discontinued from the study.***	
3.22.	Contact Lens corrected Visual Acuity (if applicable)	Perform monocular distance and near ETDRS LogMAR visual acuity test, OD & OS	[redacted]
3.23.	Exit Snellen Visual Acuity	Record the Snellen visual acuity, distance and near, OD & OS. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.	[redacted]
3.24.	Continuance	Subject in the interventional arm will continue in the study, if they must meet all three of the following criteria: • Snellen visual acuity is 20/25 or better, distance and near (OD, OS) • The lens fit is acceptable OD and OS • Investigator approval	
3.25.	Dispense (if applicable)	The lenses will be dispensed for a 6-8 day wearing period. During this time, they are required to wear the lenses at least 5 days and at least 8 hours per day that they are worn. • Dispense enough lenses to last the subject to their scheduled follow-up visit. Do not dispense extras* • The lenses will be worn as daily wear/daily disposable only • A patient instruction booklet will be provided • Subjects will be scheduled for their 1-week follow-up visit, ensuring that they wear the study lens at least 6 hours on the day of the follow-up visit * **Note:** In the event a lens is lost or damaged, the subject will return to the clinical site for replacement. As much as reasonably	

Visit 3: Treatment 2			
Step	Procedure	Details	[redacted]
		possible, a damaged lens and packaging should be returned to the clinical site (wet, if possible) and then returned to the Sponsor. If lens damage is present, complete the Product Quality Complaint Form. The lens will be stored in labeled vial with saline, and clearly differentiated from the other worn lenses that will be shipped back to the Sponsor.	
3.26.	Subject instruction	The subjects will be scheduled for Visit 4 in 6-8 days and will present after at least 6 hours of spectacle or contact lens wear time (as assigned) on the day of the visit.	

VISIT 4

The subjects must present to Visit 4, 6-8 days following Visi3 3, after at least 6 hours of wear time on the day of the visit.

Visit 4: Treatment 2 Follow-Up 1			
Step	Procedure	Details	[redacted]
4.1.	Adverse Events and Concomitant Medications Review	Review any changes to the subject's medical history or concomitant medications from the previous study visit. Record any changes, and any adverse events.	
4.2.	Wearing Time (if applicable)	Record the average wearing time and comfortable wearing time.	
4.3.	Compliance	Confirm compliance with the prescribed wear schedule.	
4.4.	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]
4.5.	Follow-Up Spectacle Questionnaires (if applicable): DEQ-5, MRD, and Digital Device	The subject will respond to the Follow-Up Questionnaire.	
4.6.	Follow-Up Contact lens Questionnaires (if applicable): CLDEQ-8, MRD, and Digital Device	The subject will respond to the Follow-Up Questionnaire.	[redacted]
4.7.	Visual Acuity	Perform monocular distance and near ETDRS LogMAR visual acuity test, OD & OS	[redacted]
4.8.	Subjective Lens Fit Assessment (if	Evaluate overall lens fit acceptance (acceptable or unacceptable) based on	[redacted]

Visit 4: Treatment 2 Follow-Up 1			
Step	Procedure	Details	[redacted]
	applicable)	centration, movement and other fitting characteristics. An unacceptable fit is deemed by one of the following criteria: • limbal exposure at primary gaze or with extreme eye movement • edge lift • excessive movement in primary and up gaze • insufficient movement in all three of the following conditions: primary gaze, up gaze, and Josephson push up **Note**: ***if lens fit is unacceptable subject will be discontinued from the study.***	
4.9.	Wettability Characteristics (if applicable)	Record the white light lens wettability of both lenses.	[redacted]
4.10.	Surface Debris & Deposits (if applicable)	Record any front and back surface lens debris and deposits.	[redacted]
4.11.	Tear film stability (Pre-Lens or Pre-Corneal as applicable) as available by site	Record the first tear film stability (NIBUT/NIKBUT), OD & OS. Record three measurements.	(Appendix E & F)
4.12.	Blink patterns (as site applicable)	Record the Blink Patterns, OD & OS	Lipiview II manufacturer instructions (Appendix G)
4.13.	Pre-corneal or Pre-lens (as applicable) tear film lipid layer thickness as available by site	Record the tear film lipid layer thickness, OD & OS	Lipiview II manufacturer instructions (Appendix G)
4.14.	Lens Removal and Storage (if applicable)	The lenses will be removed by the subject. VRC site only, both lenses will be stored dry in a labeled glass vial and frozen, using study specific labels. Otherwise, lenses will be discarded.	[redacted]
4.15.	Slit Lamp Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings	[redacted]

Visit 4: Treatment 2 Follow-Up 1			
Step	Procedure	Details	[redacted]
		If the subject has a Grade 3 slit lamp finding, it will be recorded as an Adverse Event	
4.16.	Lid wiper Epitheliopathy	Record the lid wiper epitheliopathy (upper & lower) by Lissamine green, OD & OS	Lid Wiper Epitheliopathy Work Aid (Appendix H)
4.17.	Conjunctival staining	Record the conjunctival staining by Lissamine green, OD & OS	[redacted]
4.18.	Meibomian Gland Expressibility (Lower lid, 3 regions)	Record the Meibomian Gland Expressibility, OD & OS via Meibomian Gland Secretion Grading Scale (Appendix I)	Procedure per Meibomian Gland Evaluator manufacturer instructions. (Appendix I)
4.19.	Eye Rinse	If the clearance if dye needs to be expedited, the study investigator or technician will rinse the subject's eyes thoroughly with a study provided solution.	

FINAL EVALUATION

The final evaluation will ordinarily take place immediately following the last scheduled follow-up visit per the study protocol. It may also take place at any point the subject discontinues the study or is terminated from the study.

Final Evaluation			
Step	Procedure	Details	[redacted]
F.1	Final Exam Form	Indicate if the subject completed the study successfully. If subject discontinued from the study, indicate the reason.	
F.2	Sensitivity Questionnaire	Completed subjects will respond to a Sensitivity Questionnaire	(Appendix A)
F.3	Subjective spherocylindrical Refraction	Perform bare-eye subjective spherocylindrical refraction with a phoropter and record the best corrected distance Snellen visual acuity to the nearest letter (OD, OS).	[redacted]
F.4	Exit Slit Lamp Biomicroscopy	For discontinued subjects, FDA Slit Lamp Classification Scale will be used to grade the findings. If the clearance of dye needs to be expedited, preservative-free rewetting drops or saline may	[redacted]

Final Evaluation			
Step	Procedure	Details	[redacted]
		be instilled.	

7.3. Unscheduled Visits

If, during the investigation, a subject requires an unscheduled visit to the clinical site, the following information will be collected as applicable:

- Chief complaint prompting the visit. If the reason is an adverse event, the applicable eCRF for the adverse event must be completed and subject record completed as appropriate
- Date and time of the visit and all procedures completed at the unscheduled visit
- Review of adverse event and concomitant medications
- Documentation of any test article dispensed or collected from the subject, if applicable
- Slit lamp findings (using the Slit Lamp Classification Scale)

If the Investigator withdraws a subject from the study, the final study visit case report forms must be completed indicating the reason(s) why the subject was withdrawn. The subject record must be completed documenting the date and primary reason for withdrawal and the study CRA notified.

Any ocular and non-ocular Adverse Events that are ongoing at the time of the study visit will be followed by the Investigator, within licensure, until they have resolved, returned to pre-treatment status, stabilized, or been satisfactorily explained. If further treatment i.e., beyond licensure is required, the subject will be referred to the appropriate health care provider.

The following information will be collected during an unscheduled visit, as applicable.

Unscheduled Visit			
Step	Procedure	Details	[redacted]
U.1	Chief Complaints	Record the subject's chief complaints for reasons for the unscheduled visit.	
U.2	Adverse Events and Concomitant Medications Review	Review any changes to the subject's medical history or concomitant medications from the previous study visit. Record any changes, and any adverse events.	
U.3	Entrance VA	Record the entrance distance visual acuity (OD, OS) to the nearest letter.	[redacted]
U.4	Subjective Sphero-cylindrical Refraction	Perform bare-eye subjective spherocylindrical refraction with a phoropter and record the best corrected distance visual acuity to the nearest letter (OD, OS).	[redacted]
U.5	Slit Lamp Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops may be	[redacted]

Unscheduled Visit			
Step	Procedure	Details	[redacted]
		instilled.	
U.6	Dispensing (if applicable)	Dispenses lenses as needed	
U.7	Exit Visual Acuity	Record the subject's exit distance visual acuity (OD, OS) to the nearest letter.	[redacted]

7.4. Laboratory Procedures

Ex-vivo lenses will only be collected from the internal clinic site by the sponsor for potential analysis, under a separate protocol and/or reporting.

8. SUBJECTS COMPLETION/WITHDRAWAL

8.1. Completion Criteria

Subjects are considered to have completed the study if they:

- Provided informed consent
- Are eligible
- Completed all study visits

8.2. Withdrawal/Discontinuation from the Study

A subject will be withdrawn from the study for any of the following reasons:

- Subject death during the study period
- Subject withdrawal of consent
- Subject not compliant to protocol
- Subject lost to follow-up
- Subject no longer meets eligibility criteria (e.g. the subject becomes pregnant)
- Subject develops significant or serious adverse events causing discontinuation of study lens wear
- Subjects who have experienced a Corneal Infiltrative Event (CIE)
- Investigator's clinical judgment regarding the subject safety reasons (that it is in the best interest of the subject to stop treatment)
- Subject missed study visits
- Subject not compliant with study lens wear schedule
- Subject not successfully dispensed due to lack of efficacy and safety including poor vision, poor comfort or unacceptable fit

For discontinued subjects, the Investigator will:

- Complete the current visit (scheduled or unscheduled)
- Complete the Final Evaluation, indicating the reason that the subject was discontinued from the study
- Record the spherocylindrical refraction with best corrected distance visual acuity

- Collect used test article(s) (worn or brought to the visit) from the subject and discard them, unless otherwise stated in Section 7.2
- Collect all unused test article(s) from the subject

An additional subject will be enrolled if a subject discontinues from the study prematurely.

In cases where a subject is lost to follow-up, every possible effort must be made to contact the subject and determine the reason for discontinuation/withdrawal. The measures taken to follow up must be documented including two written attempts and a certified letter (or equivalent) as the final attempt.

9. PRE-STUDY AND CONCOMITANT INTERVENTION/MEDICATION

Concomitant medications will be documented during screening and updated during the study. Disallowed medications for this study include: Restasis, Xiidra, ocular steroids, or any medication (RX or OTC) that may interfere with contact lens wear (at the discretion of the investigator)
Concomitant therapies that are disallowed include: NA.

10. DEVIATIONS FROM THE PROTOCOL

Investigator will notify study sponsor upon identification of a protocol deviation. Major protocol deviations must be reported to the sponsor within 24 hours after discovery of the protocol deviation. The Investigator will report deviations per IRB/IEC requirements. All deviations will be tracked and corrective actions implemented as appropriate.

If it becomes necessary for the Investigator to implement a deviation in order to eliminate an immediate hazard to the trial subject, the Investigator may implement the deviation immediately without notification to the sponsor. Within 24 hours after the implemented deviation, the Investigator must notify and provide the rationale to the Sponsor and, as required, the IEC/IRB.

11. STUDY TERMINATION

The occurrence of one or more Unanticipated Serious Adverse Device Effect (USADE), or any SAE where the relationship to study agent cannot be ruled out, may result in stopping further dispensing of test article. In the event of a USADE or SAE, the Sponsor may unmask the treatment regimen for the subject(s) and will discuss this with the Investigator before any further subjects are enrolled.

The Sponsor will determine when a study will be stopped. The Principal Investigator always has the discretion to initiate stopping the study based on patient safety or if information indicates the study's results are compromised.

JJVC reserves the right to terminate the study at any time for any reason. Additionally, the IEC/IRB reserves the right to terminate the study if an unreasonable risk is determined. The

study can be terminated by the Principal Investigator at the individual clinical site due to specific clinical observations, if in their opinion, after a discussion with JJVC, it is determined that it would be unwise to continue at the clinical site.

JJVC (and the IEC/IRB and DMC, if applicable) will evaluate all adverse events. If it is determined that an adverse event presents an unreasonable risk, the investigation, or that part of the investigation presenting the risk, will be terminated, as soon as possible.

Should the study be terminated (either prematurely or as scheduled), the Investigator will notify the IEC/IRB and Regulatory Authority as required by local regulatory requirements.

12. PROCEDURE FOR HANDLING PRODUCT QUALITY COMPLAINTS

A Product Quality Complaint (PQC) refers to any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness or performance of test articles after they have been released for clinical trial use.

Potential complaints may come from a variety of sources including but not limited to subjects, clinical research associates (CRA), clinical operations managers (COM), medical monitors, and site personnel, etc. The following are not considered product quality complaints:

- Subject satisfaction inquiries reported via "Subjective Questionnaires" and "Patient Reported Outcomes (PRO)"
- Clinical test articles that are stored improperly or damaged after receipt at the investigational site
- Lens replacements that occur due to drops/fall-outs
- Damage deemed by clinicians or clinical staff to be caused by handling by the user, and not indicative of a quality deficiency (i.e. tears, rips, etc.), only in situations where there is no deficiency alleged by the subject

Within 24 hours of site personnel becoming aware that a PQC has occurred, the PQC must be recorded in the EDC system, which will trigger an automatic email notification to the appropriate COM/CRA and Clinical QA representative. In cases where the EDC system in use is not configured to send automatic notifications or when an EDC system is not used, the COM/CRA is responsible for notifying Clinical QA upon discovery that a PQC has occurred.

Upon receipt of the EDC notification, the COM/CRA will contact the study site to collect additional information which will include:

- Date the complaint was received/recorded in the EDC System (Date of Sponsor Awareness)
- Who received the complaint
- Study number
- Clinical site information (contact name, site ID, telephone number)
- Lot number(s)
- Unique Subject Identifier(s)

- Indication of who first observed complaint (site personnel or subject)
- OD/OS indication, along with whether the lens was inserted
- Any related AE number if applicable
- Detailed complaint description (scheduled/unscheduled visit, wear time, symptoms, resolution of symptoms, etc.)
- Eye Care Provider objective (slit lamp) findings if applicable
- Confirmation of product availability for return (and tracking information, if available), or rationale if product is not available for return (Refer to Form Control No. [redacted] for test article return instructions)

Once a complaint is received, it will be assessed by the COM, CRA, or trained site personnel to determine if it is an Adverse Event/Serious Adverse Event (AE/SAE). If the complaint results in an AE/SAE, the COM/CRA, or trained site personnel will follow Section 13 of this protocol. If the AE/SAE was potentially the result of a product quality related deficiency, these procedures also applies and will be executed in parallel.

In some cases, a PQC form may be generated in EDC by the site in error. In this event, the PQC forms will be marked "Intentionally Left Blank" or "ILB". Justification for ILB must be documented.

13. ADVERSE EVENTS

13.1. Definitions and Classifications

Adverse Event (AE) – An AE is "any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device.
Note 1 to entry: This definition includes events related to the investigational medical device or the comparator.
Note 2 to entry: This definition includes events related to the procedures involved.
Note 3 to entry: For users or other persons, this definition is restricted to events related to investigational medical devices."[1]

An AE includes any condition (including a pre-existing condition) that:

1. Was not present prior to the study, but appeared or reappeared following initiation of the study
2. Was present prior to the study, but worsened during the study. This would include any condition resulting from concomitant illnesses, reactions to concomitant medications, or progression of disease states
3. Pregnancy must be documented as an adverse event and must be reported to the clinical monitor and to the Sponsor immediately upon learning of the event

Serious Adverse Event (SAE) – An SAE is any untoward medical occurrence that:

- Results in death
- Is life threatening
- Requires in-patient hospitalization or prolongation of existing hospitalization

- Results in persistent or significant disability/incapacity (e.g., a sight threatening event, a significant persistent or permanent change, impairment, damage, or disruption to the subject's body)
- Is a congenital anomaly/birth defect, or
- Requires intervention to prevent permanent damage (the use of the test article resulting in a condition which requires medical or surgical intervention to preclude permanent impairment of the body structure or a body function). Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered an SAE when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in the above definition

Diagnoses and conditions that are considered Ocular Serious Adverse Events include, but not limited to:

- Microbial Keratitis (MK)
- Iritis (including cells in the anterior chamber)
- Permanent decrease in best spectacle corrected visual acuity equivalent to 2 acuity lines or greater
- Central Corneal Opacity
- Central Corneal Neovascularization
- Uveitis
- Endophthalmitis
- Hypopyon
- Hyphemia
- Penetration of Bowman's Membrane
- Persistent Epithelial Defect
- Limbal cell Damage leading to Conjunctivalization

Significant Adverse Events – Those events that are usually symptomatic and warrant discontinuation (temporary or permanent) of the test article (excluding Serious Adverse Events).

Diagnoses and conditions that are considered Ocular Significant Adverse Events include, but not limited to the following:

- Contact Lens Induced Peripheral Ulcer (CLPU)
- Significant Infiltrative Events (SIE)
- Superior Epithelial Arcuate Lesions (SEALs)
- Any Temporary Loss of > 2 Lines of BSCVA
- Other grade 3 or higher corneal findings, such as abrasions or edema
- Non-contact lens related corneal events - e.g. Epidemic Keratoconjunctivitis (EKC)
- Asymptomatic Corneal Scar
- Any corneal event which necessitates temporary lens discontinuation > 2 weeks

Non-Significant Adverse Events – Those conditions that are usually asymptomatic and usually do not warrant discontinuation (temporary or permanent) of the test article. However, the Investigator may choose to treat as a precautionary measure.

Diagnoses and conditions that are considered Ocular Non-Significant Adverse Events include, but not limited to the following:

- Non-significant Infiltrative Event (NSIE)
- Contact Lens Papillary Conjunctivitis (CLPC)
- Superficial Punctate Keratitis (SPK)
- Conjunctivitis: Bacterial, Viral, Allergic
- Blepharitis
- Meibomianitis
- Contact Dermatitis
- Localized Allergic Reactions
- Any corneal event not explicitly defined as serious or significant adverse event, which necessitates temporary lens discontinuation < 2 weeks

Adverse Device Effect (ADE) – An ADE is an "adverse event related to the use of an investigational medical device.
Note 1 to entry: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.
Note 2 to entry: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device."[1]

Unanticipated Adverse Device Effect (UADE) – Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, the test article, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan, Investigator's Brochure or protocol, or any other unanticipated serious problem associated with the test article that relates to the rights, safety and welfare of subjects.

13.2. Assessing Adverse Events

In conjunction with the medical monitor, the Investigator will evaluate adverse events to ensure the events are categorized correctly. Elements of categorization will include:

- Seriousness/Classifications (see definition in Section 13.1)
- Causality or Relatedness – i.e. the relationship between the test article, study treatment or study procedures and the adverse event (not related; unlikely related; possibly related; related - see definition in Section 13.2.1)
- Adverse Event Severity – Adverse event severity is used to assess the degree of intensity of the adverse event (mild; moderate; severe for all events - see definition in Section 13.2.2)
- Outcome – not recovered or not resolved; recovering or resolving; recovered or resolved with sequelae; recovered or resolved; death related to adverse event; unknown

- Actions Taken – none; temporarily discontinued; permanently discontinued; other

13.2.1. Causality Assessment

Causality Assessment – A determination of the relationship between an adverse event and the test article. The test article relationship for each adverse event should be determined by the investigator using these explanations:

- Not Related- An adverse event that is not related to the use of the test article, study treatment or study procedures
- Unlikely Related – An adverse event for which an alternative explanation is more likely, e.g. concomitant treatment, concomitant disease(s), or the relationship of time suggests that a causal relationship is not likely
- Possibly Related – An adverse event that might be due to the use of the test article, or to the study treatment or study procedures. An alternative explanation, e.g. concomitant treatment, concomitant disease(s), is inconclusive. The relationship in time is reasonable. Therefore, the causal relationship cannot be excluded
- Related – An adverse event that is listed as a possible adverse effect (device) or adverse reaction (drug) and cannot be reasonably explained by an alternative explanation, e.g. concomitant treatment of concomitant disease(s). The relationship in time is very suggestive, e.g. it is confirmed by de-challenge and re-challenge

13.2.2. Severity Assessment

Severity Assessment – A qualitative assessment of the degree of intensity of an adverse event as determined by the Investigator or reported to him/her by the subject. The assessment of severity is made irrespective of test article, study treatment or study procedure relationship or seriousness of the event and should be evaluated according to the following scale:

- Mild – Event is noticeable to the subject, but is easily tolerated and does not interfere with the subject's daily activities
- Moderate – Event is bothersome, possible requiring additional therapy, and may interfere with the subject's daily activities
- Severe – Event is intolerable, necessitates additional therapy or alteration of therapy and interferes with the subject's daily activities

13.3. Documentation and Follow-Up of Adverse Events

The recording and documenting of adverse events (ocular and non-ocular) begins when the subjects are exposed to the test article, study treatment or study procedure. Adverse events reported before the use of test article, start of study treatment, or study procedures will be recorded as medical history. However, if the condition deteriorates at any time during the study it will be recorded and reported as an AE. Untoward medical events reported after the subject's exit from the study will be recorded as adverse events at the discretion of the Investigator.

Upon finding an adverse event, the Principal Investigator will document the condition in the subject record and in the eCRFs. He/she will complete the Adverse Event /eCRF.

Complete descriptions of all adverse events must be available in the subject record. All Adverse Events including local and systemic reactions not meeting the criteria for "serious adverse events" shall be captured on the appropriate case report form or electronic data system. All adverse events occurring while the subject is enrolled in the study must be documented appropriately regardless of relationship.

It is the Investigator's responsibility to maintain documentation of each reported adverse event. All adverse events will be followed in accordance with applicable licensing requirements. Such documentation will include the following:

- Adverse event (diagnosis not symptom)
- Drawings or photographs (where appropriate) that detail the finding (e.g., size, location, and depth, etc.)
- Date the clinical site was notified
- Date and time of onset
- Date and time of resolution
- Adverse event classification, severity, and relationship to test articles, as applicable
- Treatment regimen instituted, including concomitant medications prescribed, in accordance with applicable licensing requirements
- Any referral to another health care provider if needed
- Outcome, ocular damage (if any)
- Likely etiology
- Best corrected visual acuity at the discovery of the event and upon conclusion of the event

In addition, if an infiltrate(s) is present, he/she will complete the Corneal Infiltrate Assessment eCRF. Where necessary, a culture of the corneal lesion will be collected to determine if the infection is microbial in nature. If cultures are collected, the date of culture collection and laboratory utilized will be recorded.

Changes in the severity of an AE shall be documented to allow an assessment of the duration of the event at each level of intensity to be performed. Adverse events characterized as intermittent require documentation of the onset and duration of each episode. Changes in the assessment of relationship to the Test Article shall also be clearly documented.

Subjects who present with an adverse event shall be followed by the Investigator, within licensure, until all signs and symptoms have returned to pre-treatment status, stabilized, or been satisfactorily resolved. If further treatment beyond licensure is required, the patient will be referred to the appropriate health care provider. The Investigator will use his/her clinical judgment as to whether a subject reporting with an adverse event will continue in the study. If a subject is discontinued from the study, it will be the responsibility of the Investigator to record the reason for discontinuation. The Investigator will also document the adverse event appropriately and complete the Adverse Event eCRF. Any subjects with ongoing adverse events related to the test article, study treatment or study procedures, as of the final study visit date, should be followed to resolution of the adverse event or until referral to an appropriate health care provider, as recommended by the Investigator. Non-ocular adverse

events that are not related to the test article, study treatment, or study procedures may be recorded as "ongoing" without further follow-up.

13.4. Reporting Adverse Events

The Investigator will notify the Sponsor of an adverse event by e-mail, facsimile, or telephone as soon as possible and no later than 24 hours from discovery for any serious /significant adverse events, and 2 days from discovery for any non-significant adverse event. In addition, a written report will be submitted by the Principal Investigator to the IEC/IRB according to their requirements (Section 13.4.2). The report will comment whether the adverse event was considered to be related to the test article, study treatment or study procedures.

13.4.1. Reporting Adverse Events to Sponsor

Serious/Significant Adverse Events
The Investigator will inform the sponsor of all serious/significant adverse events occurring during the study period as soon as possible by e-mail, fax, or telephone, but no later than 24 hours following discovery of the event. The Investigator is obligated to pursue and obtain information requested by the Sponsor in addition to that information reported on the eCRF. All subjects experiencing a serious/significant adverse event must be followed up and all outcomes must be reported.

When medically necessary, the Investigator may break the randomization code to determine the identity of the treatment that the subject received. The Sponsor and study monitor should be notified prior to unmasking the test articles.

In the event of a serious/significant adverse event, the Investigator must:

- Notify the Sponsor immediately
- Obtain and maintain in the subject's records all pertinent medical information and medical judgment for colleagues who assisted in the treatment and follow-up of the subject
- Provide the Sponsor with a complete case history which includes a statement as to whether the event was or was not related to the use of the test article
- Notify the IEC/IRB as required by the IEC/IRB reporting procedure according to national regulations

Unanticipated (Serious) Adverse Device Effect (UADE)
In the event of an Unanticipated (Serious) Adverse Device Effect (UADE), the Investigator will submit a report of the UADE to the Sponsor and IEC/IRB as soon as possible, but no later than 24 hours after the Investigator first learns of the effect. This report is in addition to the immediate notification mentioned above.

The Sponsor must conduct an evaluation of the UADE and must report the results of the evaluation to FDA, the IEC/IRB and participating Investigators within 10 working days after the Sponsor first receives notification of the effect.

Non-Serious Adverse Events
All non-serious adverse events, including non-serious adverse device effects, will be reported to the sponsor by the Investigator no later than 2 days from discovery.

13.4.2. Reporting Adverse Events to the Responsible IEC/IRB and Health Authorities

Adverse events that meet the IEC/IRB requirements for reporting must be reported within the IEC/IRB's written guidelines. Each clinical site will refer to and follow any guidelines set forth by their Approving IEC/IRB. Each clinical site will refer to and follow any guidelines set forth by their local governing Health Authorities.

The Sponsor will report applicable Adverse Events to the local health authorities according the written guidelines, including reporting timelines.

13.4.3. Event of Special Interest

None

13.5. Reporting of Pregnancy

Subjects reporting pregnancy (by self-report) during the study will be discontinued after the event is recorded as an Adverse Event. Once discontinued, pregnant participants and their fetuses will not be monitored for study related purposes. At the Investigator's discretion, the study participant may be followed by the Investigator through delivery. However, this data will not be collected as part of the clinical study database. Pregnant participants are not discontinued from contact lens or solution related studies for safety concerns, but due to general concerns relating to pregnancy and contact lens use. Specifically, pregnant women are discontinued due to fluctuations in refractive error and/or visual acuity that occur secondary to systemic hormonal changes, and not due to unforeseen health risks to the mother or fetus.

14. STATISTICAL METHODS

14.1. General Considerations

Statistical Analysis will be undertaken by the sponsor or under the authority of the sponsor. A general description of the statistical methods to be implemented in this clinical trial is outlined below.

All data summaries and statistical analyses will be performed using the Statistical Analysis System (SAS) software Version 9.4 or higher (SAS Institute, Cary, NC). Throughout the analysis of data, the results for each subject/eye will be used when available for summarization and statistical analysis.

Summary tables (descriptive statistics and/or frequency tables) will be provided for all baseline variables, efficacy variables and safety variables as appropriate. Continuous variables will be summarized with descriptive statistics (n, mean, standard deviation [SD], median, minimum and maximum). Frequency count and percentage of subjects or eyes within each category will be provided for categorical data.

14.2. Sample Size Justification

The plan is to enroll 70 eligible subjects with a minimum target of 60 subjects to complete the study. Of the total 60 subjects, 20 subjects will be habitual spectacle users (the observational arm) and 40 subjects will be habitual contact lens users (the interventional arm). The sample size was chosen by the project team, given that this study is to gain initial insights of the performance of Test lens compared to Spectacles among different users (habitual lens users and habitual spectacle users). Therefore, the sample size was not based on any empirical sample size calculation.

The power was calculated for testing the primary hypothesis based on the selected sample size of 40 subject in the intervention arm using a 2×2 cross-over design. The calculation was performed with a 2-sided type I error of 0.05 assuming the true difference of 2 (seconds) in NIBUT between Test lens and Spectacles using a linear mixed model-based power analysis method (Stroup, 1999; 2002). Historical data from [redacted] were used to obtain the overall variance of NIBUT. The overall variance of NIBUT was about 34 based on the historical data. The intra-class correlation between measurements obtained from the same subject and eye across periods was assumed to be $ICC_{eye(subj)} = 0.5$, and the intra-class correlation between measurements obtained from the same subject across eyes and periods was assumed to be $ICC_{subj} = 0.3$. The SAS procedure PROC GLIMMIX (SAS software Version 9.4) was used to perform the calculation.

Based on the calculation, if the true difference is expected to be 2 seconds in NIBUT, the sample size of 40 subjects (80 eyes) using a 2×2 crossover design has a power of 86% to test for a significant difference between Test lens and Spectacles with a two-sided type I error of 0.05.

14.3. Analysis Populations

Safety Population:

All subjects who were administered any test article excluding subjects who drop out prior to administering any test article. At least one observation should be recorded.

Per-Protocol Population:

All subjects who have successfully completed all visits and did not substantially deviate from the protocol as determined by the trial cohort review committee prior to database hard lock (Per-Protocol Population). Justification of excluding subjects with protocol deviations in the Per-Protocol Population set will be documented in a memo to file.

Intent-to-Treat (ITT) Population:

All randomized subjects regardless of actual treatment and subsequent withdrawal from study or deviation from protocol. At least one observation should be recorded.

14.4. Level of Statistical Significance

All planned analysis for this study will be conducted with an overall type I error rate of 5%. Type I error will be controlled for multiplicity across interim analysis and final analysis.

14.5. Primary Analysis

Non-Invasive Break-Up Time / Non-Invasive Keratography Break-Up Time (in seconds)

Non-invasive tear break-up time among habitual contact lens wearers (the interventional arm) will be analyzed using a linear mixed model to compare between Test lens and Spectacles. The model will include lens type (Test lens/Spectacles), sequence of lens wear, period, subject group, and subject group by lens type interaction as fixed effects, and site and subject as random effects. Other baseline characteristics known of importance such as age and gender will be included as fixed covariates when appropriate. The covariance structure for the residual errors across different periods from the same subject and eye (R-side) will be selected based on the finite sample corrected Akaike's Information Criterion (Keselman et al. 1998). Two covariate structures will be considered: Homogenous Compound Symmetry (CS) and Unstructured covariance structure (UN). The homogeneity of the covariance structure across subject groups will be evaluated using a log-likelihood ratio test.

The null and alternative hypotheses for testing significant difference between Test lens and Spectacles among habitual lens users with respect to NIBUT/NIKBUT are presented below:

$$H_0: \mu_T - \mu_S = 0$$
$$H_a: \mu_T - \mu_S \neq 0,$$

where $\mu_T - \mu_S$ is the population mean difference (Test - Spectacles) in NIBUT/NIKBUT at 1-week follow-up.

Comparison on NIBUT/NIKBUT between Test lens and Spectacles will be carried out using a two-sided 95% confidence interval (CI) constructed of least-square means (LSM) difference from the linear mixed model (Test - Spectacles). A statistically significant difference in NIBUT/NIKBUT between Test lens and Spectacles will be concluded if the upper confidence limit of the 95% CI is below zero or the lower limit is above zero.

14.6. Secondary Analysis

Meibomian Gland Expressibility

The average of Meibomian gland expressibility Total scores will be calculated and compared between Test lens and Spectacles among habitual contact lens users (the interventional arm) at 1-week follow-up.

Conjunctival Staining

The average grades of conjunctival staining will be calculated and compared between Test lens and Spectacles among habitual contact lens users (the interventional arm) at 1-week follow-up.

Lid Wiper Epitheliopathy

The proportion of eyes with clinically significant (Grade 3 or 4 for overall classification) lid wiper epitheliopathy will be calculated and compared between Test lens and Spectacles among habitual contact lens users (the interventional arm) at 1-week follow-up.

14.7. Other Exploratory Analyses

- Other exploratory endpoints will be analyzed descriptively to compare Test lens and Spectacles among habitual lens users (the interventional arm).

- Further comparisons will be conducted between Test lens/Spectacles for habitual lens users and Spectacles for habitual spectacle users with respect to all endpoints. The first period data from habitual lens users (the interventional arm) and all data from habitual spectacle users (the observational arm) will be used to analyze these endpoints descriptively.

14.8. Interim Analysis

No interim analysis is planned for this study.

14.9. Procedure for Handling Missing Data and Drop-Outs

Missing or spurious values will not be imputed. The count of missing values will be included in the summary tables and listings.

Subject dropout is expected to be one of the main reasons of missing data in this clinical trial. Past clinical trials don't provide the evidence that subject dropout is systematic or not-at-random. To evaluate the impact of missing data, sensitivity analysis will be conducted using multiple imputation methods if the proportion of subject dropout is greater than the 15%.

14.10. Procedure for Reporting Deviations from Statistical Plan

The analysis will be conducted according to that specified in above sections. There are no known reasons for which it is planned to deviate from these analysis methods. If for any reason a change is made, the change will be documented in the study report along with a justification for the change.

15. DATA HANDLING AND RECORD KEEPING/ARCHIVING

15.1. Electronic Case Report Form/Data Collection

The data for this study will be captured on electronic case report forms (eCRFs) using an EDC system (Bioclinica). An authorized data originator will enter study data into the eCRFs using the EDC system. Data collected on equipment that is not captured in EDC will be formatted to the specification of the JJVC database manager and sent to JJVC for analysis.

External Date Sources for this study include: Nightly text messaging comfort scores. These will be analyzed by the sponsor and included in the CSR.

The clinical data will be recorded on dedicated eCRFs specifically designed to match the study procedures for each visit. Once completed, the eCRFs will be reviewed for accuracy and completeness and signed by the Investigator. The sponsor or sponsor's representatives will be authorized to gain access to the subject recordation for the purposes of monitoring and auditing the study.

Edit checks, electronic queries, and audit trails are built into the system to ensure accurate and complete data collection. Data will be transmitted from the clinical site to a secure central database as forms are completed or updated, ensuring information accuracy, security, and confidentiality. After the final database lock, the Investigator will be provided with Individual Patient Profiles (IPP) including the full audit trail on electronic media in PDF format for all of the study data. The IPP must be retained in the study files as a certified copy of the source data for the study.

The content and structure of the eCRFs are compliant with ISO14155:2011.[1]

15.2. Subject Record

At a minimum, subject record should be available for the following:

- subject identification
- eligibility
- study identification
- study discussion
- provision of and date of informed consent
- visit dates
- results of safety and efficacy parameters as required by the protocol
- a record of all adverse events
- follow-up of adverse events
- medical history and concomitant medication
- test article receipt/dispensing/return records
- date of study completion
- reason for early discontinuation of test article or withdrawal from the study, if applicable

The subject record is the eCRF or an external record. The author of an entry in the subject record must be identifiable. The first point of entry is considered to be the source record.

Adverse event notes must be reviewed and initialed by the Investigator.

16. DATA MANAGEMENT

16.1. Access to Source Data/Document

The Investigator/Institution will permit trial-related monitoring, audits, IEC/IRB review and regulatory inspection(s) by providing direct access to source data/documents. Should the

clinical site be contacted for an audit by an IEC/IRB or regulatory authority, JJVC must be contacted and notified in writing within 24 hours.

16.2. Confidentiality of Information

Information concerning the investigational product and patent application processes, scientific data or other pertinent information is confidential and remains the property of JJVC. The Investigator may use this information for the purposes of the study only. It is understood by the Investigator that JJVC will use information developed in this clinical study in connection with the development of the investigational product and therefore may disclose it as required to other clinical investigators and to regulatory agencies. In order to allow the use of the information derived from this clinical study, the Investigator understands that he/she has an obligation to provide complete test results and all data developed during this study to the Sponsor.

16.3. Data Quality Assurance

Steps will be taken to ensure the accuracy and reliability of data, include the selection of qualified investigators and appropriate clinical sites and review of protocol procedures with the Principal Investigator. The Principal Investigator, in turn, must ensure that all Sub-Investigators and clinical site personnel are familiar with the protocol and all study-specific procedures and have appropriate knowledge of the study article.

Training on case report form completion will be provided to clinical site personnel before the start of the study. The Sponsor will review case report forms for accuracy and completeness remotely during the conduct of the study, during monitoring visits, and after transmission to data management. Any data discrepancies will be resolved with the Investigator or designee, as appropriate.

Quality Assurance representatives from JJVC may visit clinical sites to review data produced during the study and to access compliance with applicable regulations pertaining to the conduct of clinical trials. The clinical sites will provide direct access to study-related source data/documents and reports for the purpose of monitoring and auditing by JJVC and for inspection by local and regulatory authorities.

17. MONITORING

The study monitors will maintain close contact with the Principal Investigator and the Investigator's designated clinical site personnel. The monitor's responsibilities will include:

- Ensuring that the investigation is being conducted according to the protocol, any subsequent amendments, and regulatory requirements are maintained
- Ensuring the rights and wellbeing of subjects are protected
- Ensuring adequate resources, including facilities, laboratories, equipment, and qualified clinical site personnel
- Ensuring that protocol deviations are documented with corrective action plans, as applicable
- Ensuring that the clinical site has sufficient test article and supplies

- Clarifying questions regarding the study
- Resolving study issues or problems that may arise
- Reviewing of study records and source documentation verification in accordance with the monitoring plan

18. ETHICAL AND REGULATORY ASPECTS

18.1. Study-Specific Design Considerations

Potential subjects will be fully informed of the risks and requirements of the study and, during the study, subjects will be given any new information that may affect their decision to continue participation. Subjects will be told that their consent to participate in the study is voluntary and may be withdrawn at any time with no reason given and without penalty or loss of benefits to which they would otherwise be entitled. Only subjects who are fully able to understand the risks, benefits, and potential adverse events of the study, and provide their consent voluntarily will be enrolled.

18.2. Investigator Responsibility

The Principal Investigator is responsible for ensuring that the clinical study is performed in accordance with the signed agreement, the investigational plan, Section 4 of the ICH E6 guidelines on Good Clinical Practice (GCP),[2] and applicable regulatory requirements. GCP is an international ethical and scientific quality standard for designing, conducting, recording, and reporting studies that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety, and well-being of study subjects are protected, consistent with the principles of the Declaration of Helsinki 64th WMA General Assembly 2013[3] and that the clinical study data are credible. The Investigator must maintain clinical study files in accordance with Section 8 of the ICH E6 guidelines on Good Clinical Practice (GCP),[2] and applicable regulatory requirements.

18.3. Independent Ethics Committee or Institutional Review Board (IEC/IRB)

Before the start of the study, the Investigator (or Sponsor when applicable) will provide the IEC/IRB with current and complete copies of the following documents (where applicable):

- Final protocol and, if applicable, amendments
- Sponsor-approved informed consent form (and any other written materials to be provided to the subjects)
- Investigator's Brochure (or equivalent information) and amendments
- Sponsor-approved subject recruitment materials
- Information on compensation for study-related injuries or payment to subjects for participation in the study
- Investigator's curriculum vitae, clinical licenses, or equivalent information (unless not required, as documented by IEC/IRB)
- Information regarding funding, name of the Sponsor, institutional affiliations, other potential conflicts of interest, and incentives for subjects
- Any other documents that the IEC/IRB requests to fulfill its obligation

This study will be undertaken only after IEC/IRB has given full approval of the final protocol, amendments (if any), the informed consent form, applicable recruiting materials, and subject compensation programs, and the Sponsor has received a copy of this approval. This approval letter must be dated and must clearly identify the documents being approved.

During the study, the Investigator (or Sponsor when applicable) will send the following documents to the IEC/IRB for their review and approval, where appropriate:

- Protocol amendments
- Revision(s) to informed consent form and any other written materials to be provided to subjects
- If applicable, new or revised subject recruitment materials approved by the Sponsor
- Revisions to compensation for study-related injuries or payment to subjects for participation in the study
- Investigator's Brochure amendments or new edition(s)
- Summaries of the status of the study (at least annually or at intervals stipulated in guidelines of the IEC/IRB)
- Reports of adverse events that are serious, unanticipated, and associated with the test articles, according to the IRB's requirements
- New information that may adversely affect the safety of the subjects or the conduct of the study
- Major protocol deviations as required by the IEC/IRB
- Report of deaths of subjects under the Investigator's care
- Notification if a new Investigator is responsible for the study at the clinical site
- Any other requirements of the IEC/IRB

For protocol amendments that increase subject risk, the amendment and applicable informed consent form revisions must be submitted promptly to the IEC/IRB for review and approval before implementation of the change(s).

At least once a year, the IEC/IRB will review and reapprove this clinical study. This request should be documented in writing.

At the end of the study, the Investigator (or Sponsor where required) will notify the IEC/IRB about the study completion. Documentation of this notification must be retained at the clinical site and a copy provided to the CRO or Sponsor as applicable.

18.4. Informed Consent

Each subject must give written consent according to local requirements after the nature of the study has been fully explained. The consent form must be signed before performance of any study-related activity. The consent form that is used must be approved by both the Sponsor and by the reviewing IEC/IRB. The informed consent is in accordance with principles that originated in the Declaration of Helsinki,[3] current ICH[2] and ISO 14155[1] guidelines, applicable regulatory requirements, and Sponsor Policy.

Before entry into the study, the Investigator or an authorized member of the clinical site personnel must explain to potential subject the aims, methods, reasonably anticipated benefits, and potential hazards of the study, and any discomfort it may entail. Subjects will be informed that their participation is voluntary and that they may withdraw consent to participate at any time.

The subject will be given sufficient time to read the informed consent form and the opportunity to ask questions. After this explanation and before entry into the study, consent should be appropriately recorded by means of the subject's dated signature. After having obtained the consent, a copy of the informed consent form must be given to the subject.

18.5. Privacy of Personal Data

The collection, processing and disclosure of personal data and medical information related to the Study Subject, and personal data related to Principal Investigator and any clinical site personnel (e.g., name, clinic address and phone number, curriculum vitae) is subject to compliance with the Health Information Portability and Accountability Act (HIPAA) in the United States[4] /Data Protection Act in the United Kingdom[6] /insert applicable country specific regulations and add the appropriate reference in Section 22 and other applicable personal data protection and security laws and regulations. Appropriate measures will be employed to safeguard these data, to maintain the confidentiality of the person's related health and medical information, to properly inform the concerned persons about the collection and processing of their personal data, to grant them reasonable access to their personal data and to prevent access by unauthorized persons.

All information obtained during the course of the investigation will be regarded as confidential. All personal data gathered in this trial will be treated in strictest confidence by Investigators, monitors, Sponsor's personnel and IEC/IRB. No data will be disclosed to any third party without the express permission of the subject concerned, with the exception of Sponsor personnel (monitor, auditor), IEC/IRB and regulatory organizations in the context of their investigation related activities that, as part of the investigation will have access to the CRFs and subject records.

The collection and processing of personal data from subjects enrolled in this study will be limited to those data that are necessary to investigate the efficacy, safety, quality, and utility of the investigational product(s) used in this study.

These data must be collected and processed with adequate precautions to ensure confidentiality and compliance with applicable data privacy protection laws and regulations. The Sponsor ensures that the personal data will be:

- processed fairly and lawfully
- collected for specified, explicit, and legitimate purposes and not further processed in a way incompatible with these purposes
- adequate, relevant, and not excessive in relation to said purposes
- accurate and, where necessary, kept current

Explicit consent for the processing of personal data will be obtained from the participating subject before collection of data. Such consent should also address the transfer of the data to other entities and to other countries.

The subject has the right to request through the Investigator access to his personal data and the right to request rectification of any data that are not correct or complete. Reasonable steps should be taken to respond to such a request, taking into consideration the nature of the request, the conditions of the study, and the applicable laws and regulations.

Appropriate technical and organizational measures to protect the personal data against unauthorized disclosures or access, accidental or unlawful destruction, or accidental loss or alteration must be put in place. Sponsor personnel whose responsibilities require access to personal data agree to keep the identity of study subjects confidential.

19. STUDY RECORD RETENTION

In compliance with the ICH/GCP guidelines,[2] the Investigator/Institution will maintain all CRFs and all subject records that support the data collected from each subject, as well as all study documents as specified in ICH/GCP[2] and all study documents as specified by the applicable regulatory requirement(s). The Investigator/Institution will take measures to prevent accidental or premature destruction of these documents.

Essential documents must be retained until at least two (2) years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or until at least two (2) years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents will be retained for a longer period if required by the applicable regulatory requirements or instructed by the Sponsor. It is the responsibility of the Sponsor to inform the Investigator/Institution as to when these documents no longer need to be retained.

If the responsible Investigator retires, relocates, or for other reasons withdraws from the responsibility of keeping the study records, custody must be transferred to a person who will accept the responsibility. The Sponsor must be notified in writing of the name and address of the new custodian. Under no circumstance shall the Investigator relocate or dispose of any study documents before having obtained written approval from the Sponsor.

If it becomes necessary for the Sponsor or the appropriate regulatory authority to review any documentation relating to this study, the Investigator must permit access to such reports.
If the Investigator has a question regarding retention of study records, he/she should contact JJVC.

20. FINANCIAL CONSIDERATIONS

Remuneration for study services and expenses will be set forth in detail in the Clinical Research Agreement. The Research Agreement will be signed by the Principal Investigator and a JJVC management representative prior to study initiation.

JJVC reserves the right to withhold remuneration for costs associated with protocol violations such as:

- Continuing an ineligible subject in the study
- Scheduling a study visit outside the subject's acceptable visit range

JJVC reserves the right to withhold final remuneration until all study related activities have been completed, such as:

- Query resolution
- Case Report Form signature
- Completion of any follow-up action items

21. PUBLICATION

This study will be registered on ClinicalTrials.gov by the Sponsor.

22. REFERENCES

1. ISO 14155:2011: Clinical Investigation of Medical Devices for Human Subjects — Good Clinical Practice. Available at: https://www.iso.org/standard/45557.html
2. International Conference on Harmonization Good Clinical Practice E6 (ICH-GCP). Available at: http://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html
3. Declaration of Helsinki - Ethical principles for Medical Research Involving Human Subjects. Available at: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/
4. United States (US) Code of Federal Regulations (CFR). Available at: https://www.gpo.gov/fdsys/browse/collectionCfr.action?collectionCode=CFR
5. *Health Information Portability and Accountability Act (HIPAA).* Available at: https://www.hhs.gov/hipaa/for-professionals/privacy/index.html
6. *Data Protection Act. Available at:* http://www.legislation.gov.uk/ukpga/1998/29/contents
7. [redacted]
8. Stroup, W. W. 1999. Mixed model procedures to assess power, precision, and sample sizes. *The Design of Experiments 1999 Proceedings of the Biopharmaceutical Section*. Alexandria, VA: American Statistical Association, pp. 15-24.
9. Stroup, W. W. 2002. Power analysis based on spatial effects mixed models: A tool for comparing design and analysis strategies in the presence of spatial variability. *Journal of Agricultural, Biological, and Environmental Statistics 7*, 491-511.

APPENDIX A: PATIENT REPORTED OUTCOMES (STUDY QUESTIONNAIRES)

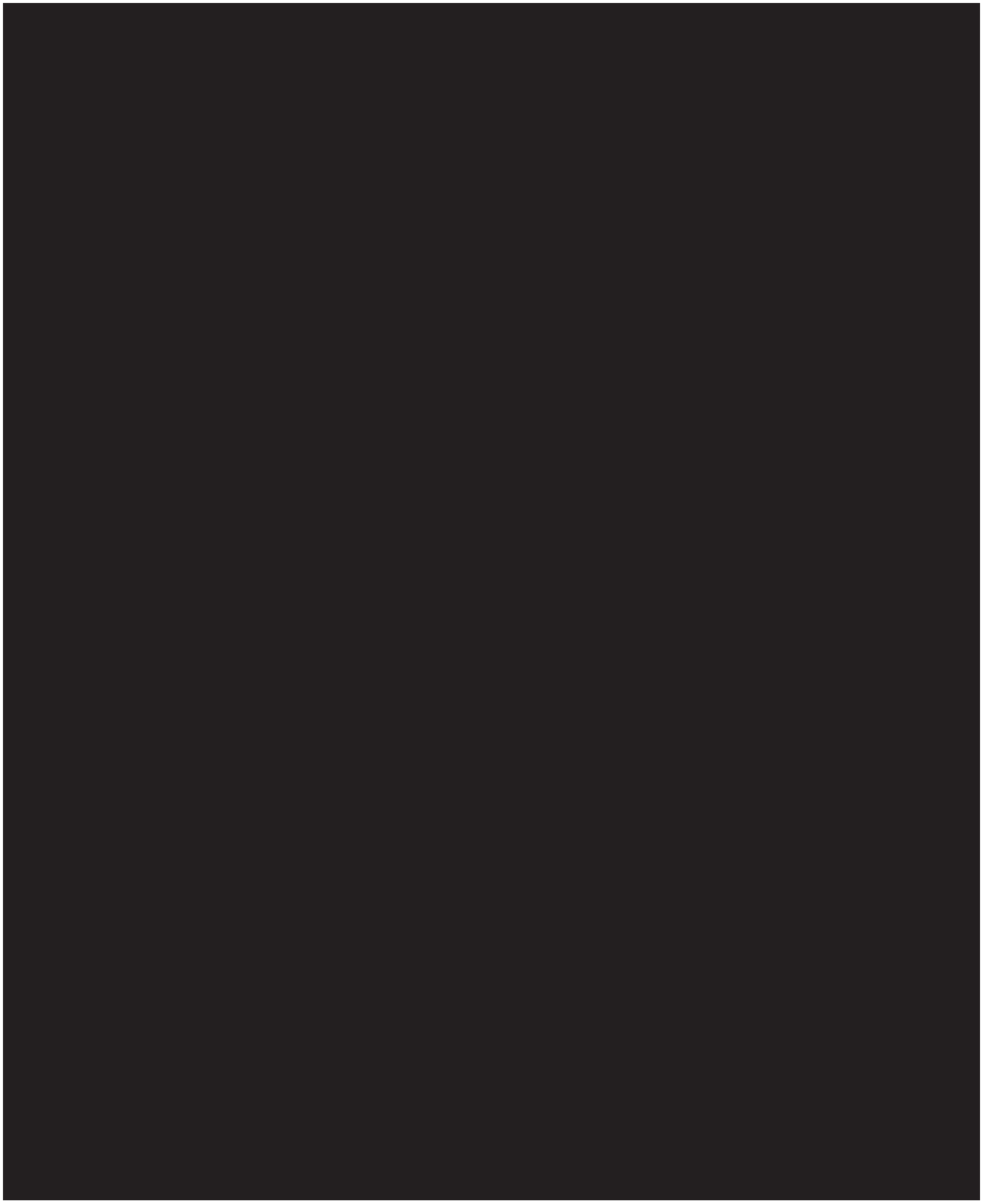
[redacted]

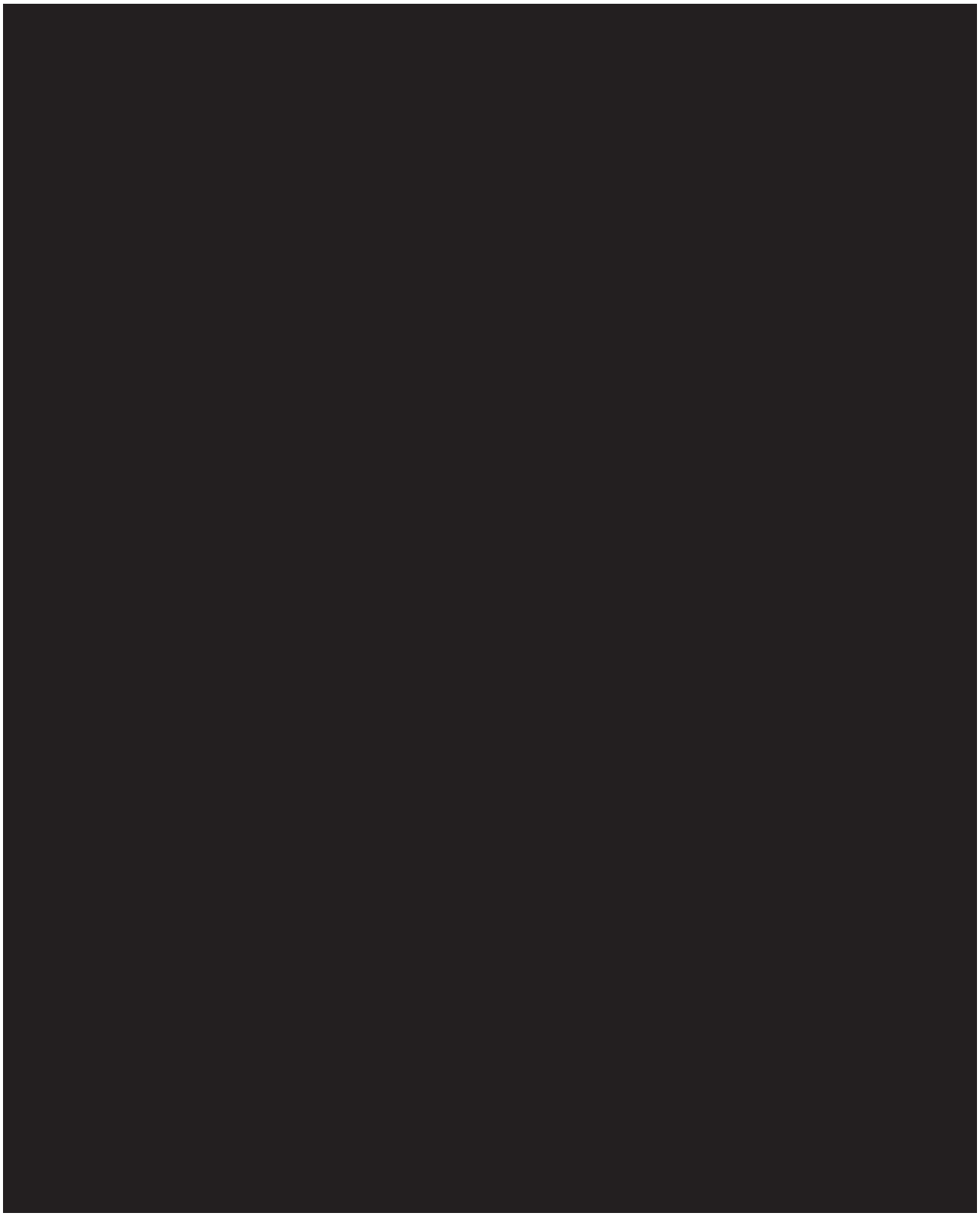
[redacted]

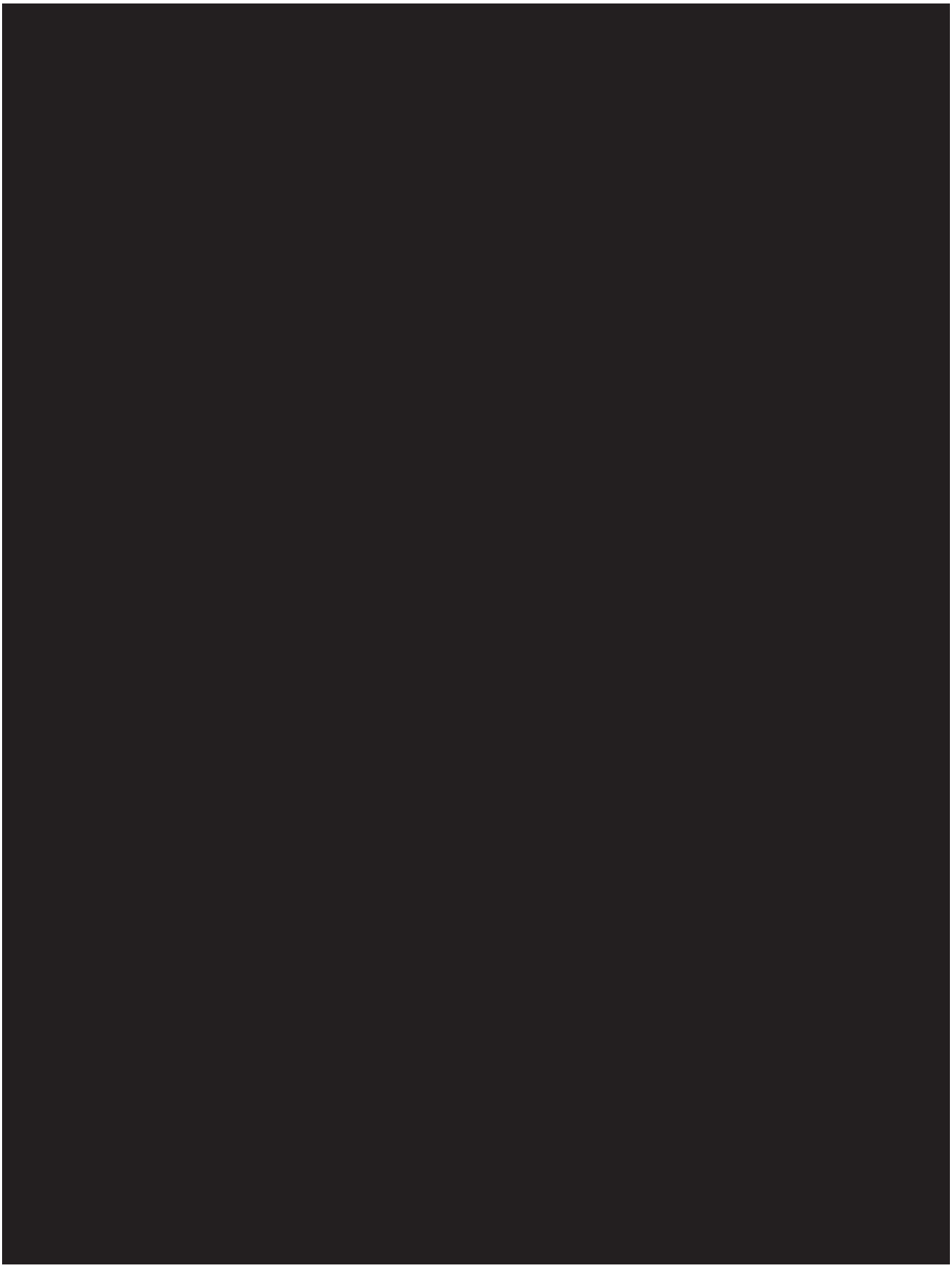
[redacted]

[redacted]

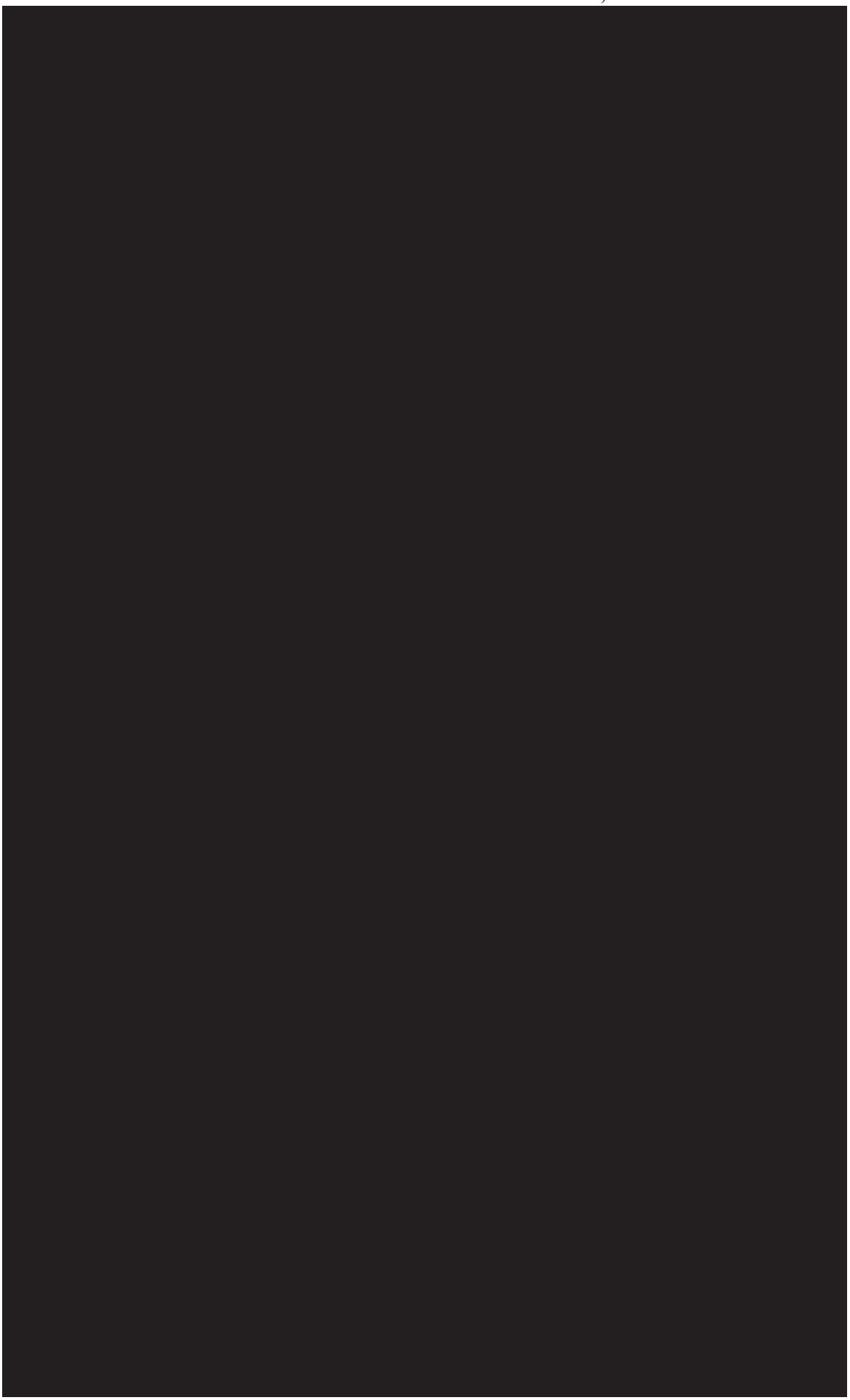
[redacted]

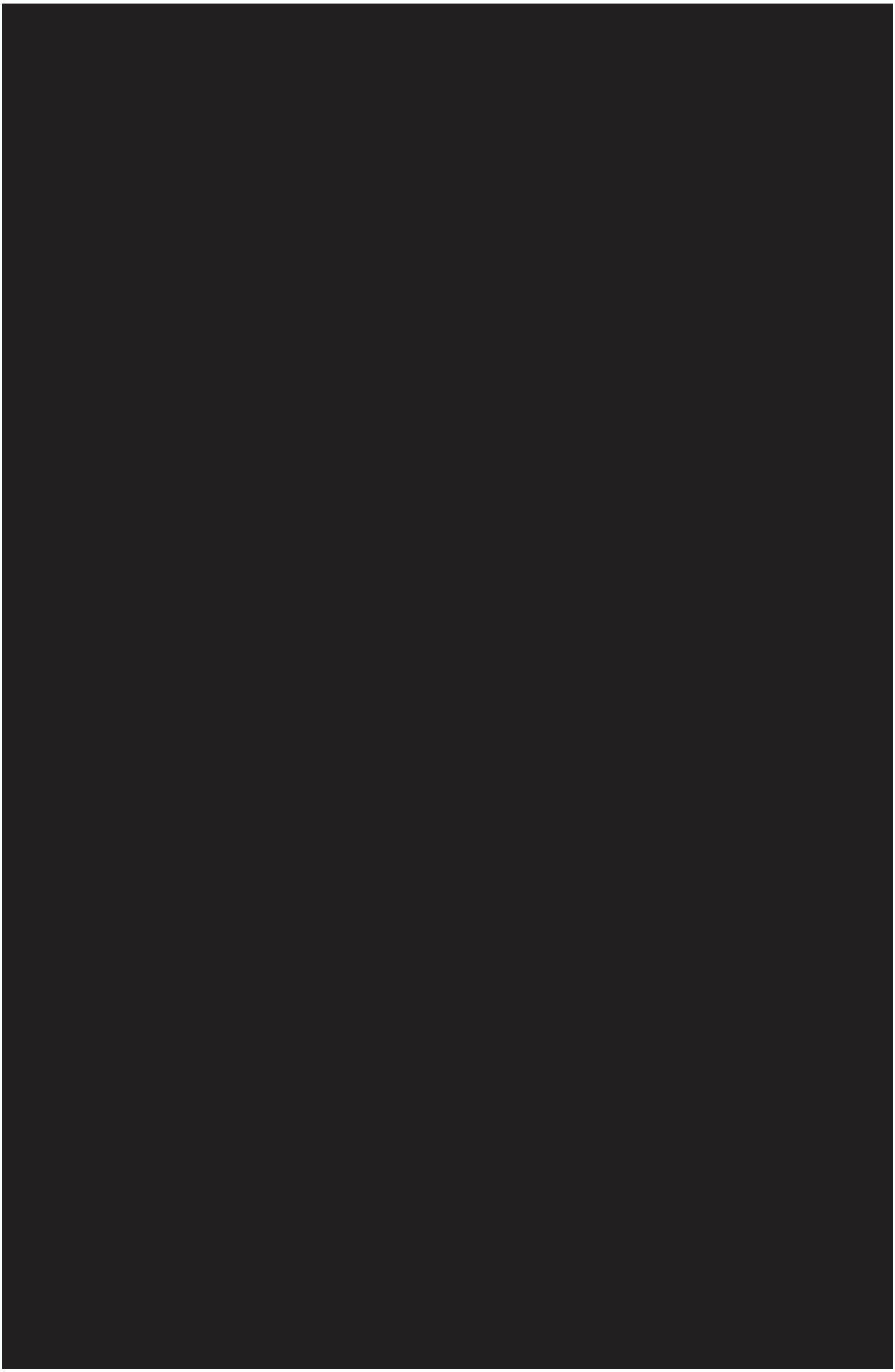






[redacted]





APPENDIX B: PATIENT INSTRUCTION GUIDE

Patient Instruction Guide (PIG) will be provided separately.

APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT)

IMPORTANT: Please read carefully and keep this information for future use.

This Package Insert and Fitting Guide is intended for the Eye Care Professional, but should be made available to patients upon request.

The Eye Care Professional should provide the patient with the appropriate instructions that pertain to the patient's prescribed lenses. Copies are available for download at www.acuvue.com.

ACUVUE® 1-Day
oasys WITH HydraLuxe™
BRAND CONTACT LENSES

ACUVUE OASYS® Brand Contact Lenses 1-Day with HydraLuxe™ Technology

ACUVUE OASYS® Brand Contact Lenses 1-Day with HydraLuxe™ Technology for ASTIGMATISM

senofilcon A Soft (hydrophilic) Contact Lenses Visibility Tinted with UV Blocker for Daily Disposable Wear

℞ Only CAUTION: U.S. Federal law restricts this device to sale by or on the order of a licensed practitioner.

SYMBOLS KEY

The following symbols may appear on the label or carton:

SYMBOL	DEFINITION
	Consult Instructions for Use
	Manufactured by or in
	Date of Manufacture
	Use By Date (expiration date)
LOT	Batch Code
STERILE 	Sterile Using Steam or Dry Heat
	Single-Use
DIA	Diameter
BC	Base Curve
D	Diopter (lens power)
CYL	Cylinder
AXIS	Axis
CE 0086	Quality System Certification Symbol
 UV Blocking	UV-Blocking
	Fee Paid for Waste Management
Rx Only	CAUTION: U.S. Federal law restricts this device to sale by or on the order of a licensed practitioner
	Lens Orientation Correct
	Lens Orientation Incorrect (Lens Inside Out)

DESCRIPTION

ACUVUE OASYS® Brand Contact Lenses 1-Day and ACUVUE OASYS® Brand Contact Lenses 1-Day for ASTIGMATISM are soft (hydrophilic) contact lenses made with HydraLuxe™ Technology. They are available as spherical or toric lenses respectively.

These lenses are made of a silicone hydrogel material containing an internal wetting agent, visibility tint, and UV absorbing monomer and are tinted blue using Reactive Blue Dye #4 to make the lenses more visible for handling.

A benzotriazole UV absorbing monomer is used to block UV radiation. The transmittance characteristics for these lenses are less than 1% in the UVB range of 280 nm to 315 nm and less than 10% in the UVA range of 316 nm to 380 nm for the entire power range.

Lens Properties:

The physical/optical properties of the lens are:

- Specific Gravity (calculated): 0.98 - 1.12
- Refractive Index: 1.42
- Light Transmission: 85% minimum
- Surface Character: Hydrophilic
- Water Content: 38%
- Oxygen Permeability:

VALUE	METHOD
122 x 10^{-11} (cm^2/sec) (ml O_2/ml x mm Hg) at 35°C	Fatt (boundary corrected, non-edge corrected)
103 x 10^{-11} (cm^2/sec) (ml O_2/ml x mm Hg) at 35°C	Fatt (boundary corrected, edge corrected)

Lens Parameters:

- Diameter Range: 12.0 mm to 15.0 mm
- Center Thickness: varies with power
- Base Curve Range: 7.85 mm to 10.00 mm
- Spherical Power Range: -20.00D to +20.00D
- Cylinder Power Range: -0.25D to -10.00D
- Axis Range: 2.5° to 180°

AVAILABLE LENS PARAMETERS

ACUVUE OASYS® Brand 1-Day with HydraLuxe™ Technology are hemispherical shells of the following dimensions:

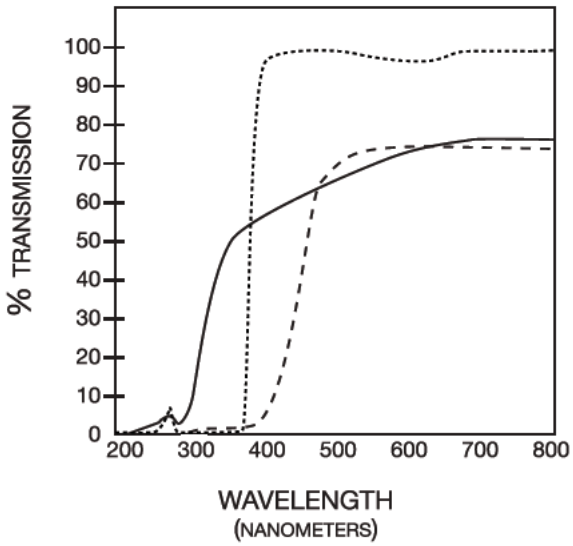
Diameter:	14.3 mm
Center Thickness:	0.085 mm to 0.221 mm (varies with power)
Base Curve:	8.5 mm, 9.0 mm
Powers:	-0.50D to -6.00D (in 0.25D increments) -6.50D to -12.00D (in 0.50D increments) +0.50D to +6.00D (in 0.25D increments) +6.50D to +8.00D (in 0.50D increments)

ACUVUE OASYS® Brand 1-Day with HydraLuxe™ Technology for ASTIGMATISM are hemitoric shells of the following dimensions:

Diameter:	14.3 mm
Center Thickness:	0.075 mm to 0.172 mm (varies with power)
Base Curve:	8.5 mm
Powers:	+0.00D to -6.00D (in 0.25D increments) Cylinders: -0.75D, -1.25D, -1.75D, -2.25D* Axis: 10° to 180° in 10° increments *-2.25D cylinder is availble in 10°, 20°, 70°, 80°, 90°, 100°, 110°, 160°, 170°, 180° axes only. +0.25D to +4.00D (in 0.25D increments) -6.50D to -9.00D (in 0.50D increments) Cylinders: -0.75D, -1.25D, -1.75D Axis: 10°, 20°, 70°, 80°, 90°, 100°, 110°, 160°, 170°, 180°

TRANSMITTANCE CURVES

ACUVUE OASYS® 1-Day with HydraLuxe™ Technology (senofilcon A) Visibility Tinted with UV Blocker vs. 24 yr. old human cornea and 25 yr. old human crystalline lens.



ACUVUE OASYS® 1-Day with HydraLuxe™ Technology (senofilcon A)*

24 YR. OLD HUMAN CORNEA[1]

25 YR. OLD HUMAN CRYSTALLINE LENS[2]

* The data was obtained from measurements taken through the central 3-5 mm portion for the thinnest marketed lens (-9.00D lens, 0.075 mm center thickness).

[1]Lerman, S., Radiant Energy and the Eye, MacMillan, New York, 1980, p. 58, figure 2-21

[2]Waxler, M., Hitchins, V.M., Optical Radiation and Visual Health, CRC Press, Boca Raton, Florida, 1986, p. 19, figure 5

WARNING: UV absorbing contact lenses are NOT substitutes for protective UV absorbing eyewear, such as UV absorbing goggles or sunglasses because they do not completely cover the eye and surrounding area. The patient should continue to use UV absorbing eyewear as directed.

ACTIONS

In its hydrated state, the contact lens, when placed on the cornea, acts as a refracting medium to focus light rays onto the retina.

The transmittance characteristics for these lenses are less than 1% in the UVB ran [redacted] m to 315 nm[redacted]

NOTE: Long-term exposure to UV radiation is one of the risk factors associated with cataracts. Exposure is based on a number of factors such as environmental conditions (altitude, geography, cloud cover) and personal factors (extent and nature of outdoor activities). UV-Blocking contact lenses help provide protection against harmful UV radiation. However, clinical studies have not been done to demonstrate that wearing UV-Blocking contact lenses reduces the risk of developing cataracts or other eye disorders. The Eye Care Professional should be consulted for more information.

INDICATIONS (USES)

ACUVUE OASYS® Brand Contact Lenses 1-Day with HydraLuxe™ Technology are indicated for daily disposable wear for the optical correction of refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes who may have 1.00D or less of astigmatism.

ACUVUE OASYS® Brand Contact Lenses 1-Day with HydraLuxe™ Technology for ASTIGMATISM are indicated for daily disposable wear for the optical correction of refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes who may have 0.50D to 3.00D of astigmatism.

These lenses contain a UV Blocker to help protect against transmission of harmful UV radiation to the cornea and into the eye.

CONTRAINDICATIONS (REASONS NOT TO USE)

DO NOT USE these contact lenses when any of the following conditions exist:

- Acute or subacute inflammation or infection of the anterior chamber of the eye.
- Any eye disease, injury or abnormality that affects the cornea, conjunctiva, or eyelids.
- Severe insufficiency of [redacted]retion (dry eye).

- Corneal hypoesthesia (reduced corneal sensitivity).
- Any systemic disease that may affect the eye or be exaggerated by wearing contact lenses.
- Allergic reactions of ocular surfaces or adnexa that may be induced or exaggerated by wearing contact lenses or use of contact lens solutions.
- Ocular irritation due to allergic reactions which may be caused by use of contact lens solutions (i.e., rewetting drops) that contain chemicals or preservatives (such as mercury, Thimerosal, etc.) to which some people may develop an allergic response.
- Any active corneal infection (bacterial, fungal, protozoal, or viral).
- If eyes become red or irritated.

WARNINGS

Patients should be advised of the following warnings pertaining to contact lens wear:

EYE PROBLEMS, INCLUDING CORNEAL ULCERS, CAN DEVELOP RAPIDLY AND LEAD TO LOSS OF VISION; IF THE PATIENT EXPERIENCES:

- **Eye Discomfort,**
- **Excessive Tearing,**
- **Vision Changes,**
- **Loss of Vision,**
- **Eye Redness,**
- **Or Other Eye Problems,**

THE PATIENT SHOULD BE INSTRUCTED TO IMMEDIATELY REMOVE THE LENSES AND PROMPTLY CONTACT THE EYE CARE PROFESSIONAL.

- When prescribed for daily wear, patients should be instructed not to wear lenses while sleeping. Clinical studies have shown that the risk of serious adverse [redacted]s is increased when lenses are worn overnight, and that the risk of ulcerative keratitis is greater for

extended wear contact lens users than for daily wear users.[3]

- Studies have shown that contact lens wearers who are smokers have a higher incidence of adverse reactions than nonsmokers.
- Problems with contact lenses or lens care products could result in serious injury to the eye. Patients should be cautioned that proper use and care of contact lenses and lens care products are essential for the safe use of these products.
- The overall risk of ulcerative keratitis may be reduced by carefully following directions for lens care.

[3] New England Journal of Medicine, September 21, 1989; 321 (12), pp. 773-783

Specific Instructions for Use and Warnings:

- **Water Activity**

  Instructions for Use

  Do not expose contact lenses to water while wearing them.

  WARNING:
  Water can harbor microorganisms that can lead to severe infection, vision loss or blindness. If lenses have been submersed in water when participating in water sports or swimming in pools, hot tubs, lakes, or oceans, the patient should be instructed to discard them and replace them with a new pair. The Eye Care Professional should be consulted for recommendations regarding wearing lenses during any activity involving water.

PRECAUTIONS

Special Precautions for Eye Care Professionals:

- Due to the small number of patients enrolled in clinical investigation of lenses, all refractive powers, design configurations, or lens parameters available in the lens material are not evaluated in significant numbers. Consequently, when selecting an appropriate lens design and parameters, the Eye Care Professional should consider all characteristics of the lens that can affect lens performance and ocular health, including oxygen permeability, wettability, central and peripheral thickness, and [redacted]e diameter.

- The potential impact of these factors on the patient's ocular health should be carefully weighed against the patient's need for refractive correction; therefore, the continuing ocular health of the patient and lens performance on the eye should be carefully monitored by the prescribing Eye Care Professional.
- Patients who wear these lenses to correct presbyopia using mono-vision may not achieve the best corrected visual acuity for either far or near vision. Visual requirements vary with the individual and should be considered when selecting the most appropriate type of lens for each patient.
- Fluorescein, a yellow dye, should not be used while the lenses are on the eyes. The lenses absorb this dye and become discolored. Whenever fluorescein is used in eyes, the eyes should be flushed with a sterile saline solution that is recommended for in-eye use.
- Eye Care Professionals should instruct the patient to remove the lenses immediately if the eyes become red or irritated.

Eye Care Professionals should carefully instruct patients about the following care regimen and safety precautions.

Handling Precautions:

- Before leaving the Eye Care Professional's office, the patient should be able to promptly remove the lenses or should have someone else available who can remove the lenses for him or her.
- DO NOT use if the sterile blister package is opened or damaged.
- Always wash and rinse hands before handling lenses. Do not get cosmetics, lotions, soaps, creams, deodorants, or sprays in the eyes or on the lenses. It is best to put on lenses before putting on makeup. Water-based cosmetics are less likely to damage lenses than oil-based products.
- DO NOT touch contact lenses with the fingers or hands if the hands are not free of foreign materials, as microscopic scratches of the lenses may occur, causing distorted vision and/or injury to the eye.
- Carefully follow the handlin[redacted]n, removal, and wearing instructions in the "Patient Instruction Guide" for the prescribed

wearing schedule and those prescribed by the Eye Care Professional.

- Always handle lenses carefully and avoid dropping them.
- Never use tweezers or other tools to remove lenses from the lens container unless specifically indicated for that use. Slide the lens up the side of the bowl until it is free of the container.
- Do not touch the lens with fingernails.

Lens Wearing Precautions:

- If the lens sticks (stops moving) on the eye, follow the recommended directions in “Care for a Sticking (Non-Moving) Lens." The lens should move freely on the eye for the continued health of the eye. If non-movement of the lens continues, the patient should be instructed to immediately consult his or her Eye Care Professional.
- Never wear lenses beyond the period recommended by the Eye Care Professional.
- The patient should be advised to never allow anyone else to wear their lenses. They have been prescribed to fit their eyes and to correct their vision to the degree necessary. Sharing lenses greatly increases the chance of eye infections.
- If aerosol products, such as hair spray, are used while wearing lenses, exercise caution and keep eyes closed until the spray has settled.
- Avoid all harmful or irritating vapors and fumes while wearing lenses.
- Always discard lenses worn as prescribed by the Eye Care Professional.

Lens Care Precautions:

- The patient should be informed that no cleaning or disinfection is needed when lenses are worn for daily disposable wear. Patients should always dispose of lenses when removed and have spare lenses or spectacles available.

Other Topics to Discuss with Patients:

- Always contact the Eye Care Professional before using any medicine in the eyes.
- Certain medications, such as antihistamines, decongestants, diuretics, muscle relaxants, tranquilizers, and those for motion sickness may cause dryness of the eye, increased lens awareness, or blurred vision. Should such conditions exist, proper remedial measures should be prescribed. Depending on the severity, this could include the use of lubricating drops that are indicated for use with soft contact lenses or the temporary discontinuance of contact lens wear while such medication is being used.
- Oral contraceptive users could develop visual changes or changes in lens tolerance when using contact lenses. Patients should be cautioned accordingly.
- As with any contact lens, follow-up visits are necessary to assure the continuing health of the patient's eyes. The patient should be instructed as to a recommended follow-up schedule.

Who Should Know That the Patient is Wearing Contact Lenses?

- Patients should inform all doctors (Health Care Professionals) about being a contact lens wearer.
- Patients should always inform their employer of being a contact lens wearer. Some jobs may require use of eye protection equipment or may require that the patient not wear contact lenses.

ADVERSE REACTIONS

The patient should be informed that the following problems may occur when wearing contact lenses:

- The eye may burn, sting, and/or itch.
- There may be less comfort than when the lens was first placed on the eye.
- There may be a feeling of something in the eye (foreign body, scratched area).

- There may be the potential for some temporary impairment due to

peripheral infiltrates, peripheral corneal ulcers, or corneal erosion. There may be the potential for other physiological observations, such as local or generalized edema, corneal neovascularization, corneal staining, injection, tarsal abnormalities, iritis, and conjunctivitis; some of which are clinically acceptable in low amounts.

- There may be excessive watering, unusual eye secretions, or redness of the eye.
- Poor visual acuity, blurred vision, rainbows, or halos around objects, photophobia, or dry eyes may also occur if the lenses are worn continuously or for too long a time.

The patient should be instructed to conduct a simple 3-part self-examination at least once a day. They should ask themselves:

- How do the lenses feel on my eyes?
- How do my eyes look?
- Have I noticed a change in my vision?

If the patient reports any problems, he or she should be instructed to IMMEDIATELY REMOVE THE LENS. If the problem or discomfort stops, the patient should discard the lens and place a new fresh lens on the eye.

If after inserting the new lens, the problem continues, the patient should be directed to IMMEDIATELY REMOVE THE LENS AND CONTACT HIS OR HER EYE CARE PROFESSIONAL.

The patient should be instructed NOT to use a new lens as self-treatment for the problem.

The patient should be advised that when any of the above symptoms occur, a serious condition such as infection, corneal ulcer, neovascularization, or iritis may be present. He or she should be instructed to seek immediate professional identification of the problem and prompt treatment to avoid serious eye damage.

GENERAL FITTING GUIDELINES

A. Patient Selection

Patients selected to wear these lenses should be chosen based on:

- Motivation to wear lenses
- Ability to follow instructions regarding lens wear care
- General health
- Ability to adequately handle and care for the lenses
- Ability to understand the risk and benefits of lens wear

Patients who do not meet the above criteria should not be provided with contact lenses.

B. Pre-fitting Examination

Initial evaluation of the patient should begin with a thorough case history to determine if there are any contraindications to contact lens wear. During the case history, the patient's visual needs and expectations should be determined as well as an assessment of their overall ocular, physical, and mental health.

Preceding the initial selection of trial contact lenses, a comprehensive ocular evaluation should be performed that includes, but is not limited to, the measurement of distance and near visual acuity, distance and near refractive prescription (including determining the preferred reading distance for presbyopes), keratometry, and biomicroscopic evaluation.

Based on this evaluation, if it is determined that the patient is eligible to wear these lenses, the Eye Care Professional should proceed to the lens fitting instructions as outlined below.

C. Initial Power Determination

A spectacle refraction should be performed to establish the patient's baseline refractive status and to guide in the selection of the appropriate lens power. Remember to compensate for vertex distance if the refraction is greater than ±4.00D.

D. Base Curve Selection (Trial Lens Fitting)

The following trial lenses should be selected for patients regardless of keratometry readings. However, corneal curvature measurements should be performed to establish the patient's baseline ocular status.

- ACUVUE OASYS® 1-Day: 8.5 mm/14.3 mm
- ACUVUE OASYS® 1-Day for ASTIGMATISM: 8.5 mm/14.3 mm

The trial lens should be placed on each of the patient's eyes and evaluated after the patient has adjusted to the lenses.

1. Criteria of a Properly Fit Lens

   A properly fit lens will center and completely cover the cornea (i.e., no limbal exposure), have sufficient movement to provide tear exchange under the contact lens with the blink, and be comfortable. The lens should move freely when manipulated digitally with the lower lid, and then return to its properly centered position when released.

2. Criteria of a Flat Fitting Lens

   A flat fitting lens may exhibit one or more of the following characteristics: decentration, incomplete corneal coverage (i.e., limbal exposure), excessive movement with the blink, and/or edge standoff. If the lens is judged to be flat fitting, it should not be dispensed to the patient.

3. Criteria of a Steep Fitting Lens

   A steep fitting lens may exhibit one or more of the following characteristics: insufficient movement with the blink, conjunctival indentation, and resistance when pushing the lens up digitally with the lower lid. If the lens is judged to be steep fitting, it should not be dispensed to the patient.

If the initial trial base curve is judged to be flat or steep fitting, the alternate base curve, if available, should be trial fit and evaluated after the patient has adjusted to the lens. The lens should move freely when manipulated digitally with the lower lid, and then return to a properly centered position when released. If resistance is encountered when pushing the lens up, the lens is fitting tightly and should not be dispensed to the patient.

E. Final Lens Power (Spherical)

A spherical over-refraction should be performed to determine the final lens power after the lens fit is judged acceptable. The spherical over-refraction should be combined with the trial lens power to determine the final lens prescription. The patient should [redacted]e good visual acuity with the correct lens power unless there is excessive residual astigmatism.

Example 1	
Diagnostic lens:	-2.00D
Spherical over-refraction:	-0.25D
Final lens power:	-2.25D

Example 2	
Diagnostic lens:	-2.00D
Spherical over-refraction:	+0.25D
Final lens power:	-1.75D

If vision is acceptable, perform a slit lamp examination to assess adequate fit (centration and movement). If the fit is acceptable, dispense the lenses and instruct the patient to return in one week for reassessment (see dispensing and follow up information in **PATIENT MANAGEMENT**).

All patients should be supplied with a copy of the PATIENT INSTRUCTION GUIDE for these lenses. Copies are available for download at www.acuvue.com.

TORIC FITTING GUIDELINES

Although most aspects of the fitting procedure are identical for all types of soft contact lenses, including toric lenses, there are some additional steps and/or rules to follow to assure the proper fit of toric lenses.

The only new steps you must follow in prescribing ACUVUE OASYS® 1-Day for ASTIGMATISM are that you must determine the stability, repeatability, and drift angle of the lens axis so that you can prescribe the correct lens axis for the patient.

A. How to Determine Lens Cylinder and Axis Orientation

1. Locate the Orientation Marks

To help determine the proper orientation of the toric lens, you'll find two primary marks approximately 1 mm from the lens edge representing the vertical position on opposite ends of the lens at 6 and 12 o'clock (Fig. 1). Because of the lens' ballasting system, either mark can represent the vertical position – there is no "top" and "bottom" as in a prism-ballasted lens. You don't need to view both marks to assess orientation; simply look for the 6 o'clock mark as you would with a prism-ballasted lens.

Figure 1

You'll need a slit lamp biomicroscope with a 1 to 2 mm parallelepiped beam to highlight the marks when the lens is fitted to the eye. There are a number of techniques you can use to improve the visibility of the 6 o'clock mark. Using a parallelepiped beam and medium magnification (10x or 15x), slowly pan down the lens, looking just below the direct illumination at the retroilluminated area. Backlighting the mark this way should make it more visible. Sometimes manipulating the lower lid may be necessary to uncover the mark.

2. Observe Lens Rotation and Stability

Observe the position and stability of the "bottom" mark. It usually stabilizes at the 6 o'clock position. If it does, calculation of the lens power will be straightforward. The 6 o'clock position is not a "must"; however, the absolute requirement is that the axis position be stable and repeatable.

The mark may stabilize somewhat left or right (drift) of the vertical meridian and still enable you to fit a toric lens for that eye, as long as the lens always returns to the same "drift axis" position after settling. The deviation can be compensated for in the final prescription. Your objective is to ensure that whatever position the initial lens assumes near 6 o'clock, this position must be stable and repeatable. With full eye movement or heavy blink, you may see the marks swing away, but they must return quickly to the original stable position. If the lens does not return quickly, you may need to select a different lens.

3. Assessing Rotation

Imagine the eye as a clock dial and every hour represents a 30° interval. If the orientation mark of the initial lens stabilizes somewhat left or right of the vertical position, the final lens will orient on the eye with the same deviation. You can use an axis reticule in the slit lamp or use a line-scribed lens in a spectacle trial frame to measure or estimate the "drift angle" of the cylinder axis.

To compensate for this "drift", measure or estimate the "drift", then add or subtract it from the refractive axis to determine the correct cylinder axis. Use the LARS (Left Add, Right Subtract) method to determine which direction to compensate.

B. Final Lens Power

When the diagnostic lens has its axis aligned in the same meridian as the patient's refractive axis, a spherocylindrical over-refraction may be performed and visual acuity determined. However, in the case of crossed axes, such as when the diagnostic lens axis is different from the spectacle cylinder axis, it is not advisable to perform a full spherocylindrical over-refraction because of the difficulty in computing the resultant power. A spherical over-refraction without cylinder refraction may be performed.

If the required cylinder correction falls between two available cylinder powers, it is recommended to prescribe the lower cylinder power lens. See below for instructions on how to determine the final lens power.

1. For the Sphere

If sphere alone or combined sphere and cylinder Rx > ±4.00D, compensate for vertex distance. If sphere alone or combined sphere and cylinder Rx ≤ ±4.00D, vertex compensation is not necessary.

2. For the Cylinder

Adjust the axis by the drift angle using the LARS method. Choose a cylinder that is ≤ 0.50D from the refractive cylinder.

3. Case Examples

Example 1

Manifest (spectacle) refraction:
O.D. -2.50D / -1.25D x 180° 20/20
O.S. -2.00D / -1.00D x 180° 20/20

Choose a diagnostic lens for each eye with axis 180°. Place the lens on each eye and allow a minimum of 3 minutes for it to equilibrate, based on the patient's initial response to the lens. If the lens has not yet stabilized, recheck until stable.

Check the orientation of the axis mark. If the bottom axis mark is in the 6 o'clock position on both eyes, choose the appropriate cylinder as listed previously. If the lens has not yet stabilized, recheck until stable.

Here is the Rx Prescribed:
O.D. -2.50D / -1.25D x 180°
O.S. -2.00D / -0.75D x 180°

Example 2
Manifest (spectacle) refraction:
O.D. -3.00D / -1.00D x 90° 20/20
O.S. -4.75D / -2.00D x 90° 20/20

Choose diagnostic lenses of -3.00D / -0.75D x 90° for the right eye and -4.50D / -1.75D x 90° for the left eye, the nearest lenses available to the spherical power, cylinder power, and axis needed. For the left eye, since the manifest refraction called for -4.75D, compensating for vertex distance the sphere is reduced by 0.25D to -4.50D. The cylinder power will be -1.75D. Place the lens on each eye and allow a minimum of 3 minutes for it to equilibrate, based on the patient's initial response to the lens. If the lens has not yet stabilized, recheck until stable.

Right Eye

The orientation mark on the right lens rotates left from the 6 o'clock position by 10° and remains stable in this position. Compensation for this rotation should be done as follows:

Compensate the 10° axis drift by adding it to the manifest refraction axis.

Here is the Rx Prescribed:
O.D. -3.00D / -0.75D x 100°

Left Eye

The orientation mark on the left lens rotates right from the 6 o'clock position by 10° and remains stable in this position.

Compensate for the 10° axis drift by subtracting it from the manifest refraction axis.

Here is the Rx Prescribed:
O.S. -4.50D / -1.75D x 80°

If vision is acceptable, perform a slit lamp examination to assess adequate fit (centration and movement). If fit is acceptable, dispense the lenses instructing the patient to return in one week for reassessment (see dispensing and follow-up information in PATIENT MANAGEMENT).

All patients should be supplied with a copy of the PATIENT INSTRUCTION GUIDE for these lenses. Copies are available for download at www.acuvue.com.

MONOVISION FITTING GUIDELINES

A. Patient Selection

1. Monovision Needs Assessment

For a good prognosis, the patient should have adequately corrected distance and near visual acuity in each eye. The amblyopic patient or the patient with significant astigmatism (greater than 1.00D) in one eye may not be a good candidate for monovision correction with these lenses.

Occupational and environmental visual demands should be considered. If the patient requires critical vision (visual acuity and stereopsis), it should be determined by trial whether this patient can function adequately with monovision correction. Monovision contact lens wear may not be optimal for activities such as:

- visually demanding situations such as operating potentially dangerous machinery or performing other potentially hazardous activities; and
- driving automobiles (e.g., driving at night). Patients who cannot meet state driver's licensing requirements with monovision correction should be advised to not drive with this correction, OR may require that additional over-correction be prescribed.

2. Patient Education

All patients do not function equally well with monovision correction. Patients may not perform as well for certain tasks with this correction as they have with spectacles (multifocal, bifocal, trifocal, readers, progressives). Each patient should understand that monovision, as well as other presbyopic alternatives, can create a vision compromise that may reduce visual acuity and depth perception for distance and near tasks. Therefore, caution should be exercised when the patient is wearing the correction for the first time until they are familiar with the vision provided in visually challenging environments (e.g., reading a menu in a dim restaurant, driving at night in rainy/foggy conditions, etc.). During the fitting process, it is necessary for the patient to realize the disadvantages as well as the advantages of clear near vision and straight ahead and upward gaze that monovision contact lenses provide.

B. Eye Selection

1. Ocular Preference Determination Methods

Generally, the non-dominant eye is corrected for near vision. The following two methods for eye dominance can be used.

Method 1: Determine which eye is the “sighting eye.” Have the patient point to an object at the far end of the room. Cover one eye. If the patient is still pointing directly at the object, the eye being used is the dominant (sighting) eye.

Method 2: Determine which eye will accept the added power with the least reduction in vision. Place a hand-held trial lens equal to the spectacle near ADD in front of one eye and then the other while the distance refractive error correction is in place for both eyes. Determine whether the patient functions best with the near ADD lens over the right or left eye.

2. Other Eye Selection Methods

Other methods include the "Refractive Error Method" and the "Visual Demands Method."

Refractive Error Method

For anisometropic correction, it is generally best to fit the more hyperopic (less myopic) eye for distance and the more myopic (less hyperopic) eye for near.

Visual Demands Method

Consider the patient’s occupation during the eye selection process to determine the critical vision requirements. If a patient’s gaze for near tasks is usually in one direction, correct the eye on that side for near.

Example: A secretary who places copy to the left side of the desk will function best with the near lens on the left eye.

C. Special Fitting Characteristics

1. Unilateral Vision Correction

There are circumstances where only one contact lens is required. As an example, an emmetropic patient would only require a near lens, whereas a bilateral myope would require corrective lenses on

both eyes.

Examples:

A presbyopic emmetropic patient who requires a +1.75D ADD would have a +1.75D lens on the near eye and the other eye left without correction.

A presbyopic patient requiring a +1.50D ADD who is -2.50D myopic in the right eye and -1.50D myopic in the left eye may have the right eye corrected for distance and the left uncorrected for near.

2. Near ADD Determination

Always prescribe the lens power for the near eye that provides optimal near acuity at the midpoint of the patient's habitual reading distance. However, when more than one power provides optimal reading performance, prescribe the least plus (most minus) of the powers.

3. Trial Lens Fitting

A trial fitting is performed in the office to allow the patient to experience monovision correction. Lenses are fit according to the GENERAL FITTING GUIDELINES for base curve selection described in this Package Insert.

Case history and standard clinical evaluation procedure should be used to determine the prognosis. Determine the distance correction and the near correction. Next determine the near ADD. With trial lenses of the proper power in place, observe the reaction to this mode of correction.

Allow the lenses to settle for about 20 minutes with the correct power lenses in place. Walk across the room and have the patient look at you. Assess the patient's reaction to distance vision under these circumstances. Then have the patient look at familiar near objects such as a watch face or fingernails. Again assess the reaction. As the patient continues to look around the room at both near and distance objects, observe the reactions. Only after these vision tests are completed should the patient be asked to read print. Evaluate the patient's reaction to large print (e.g., typewritten copy) at first and then graduate to newsprint and finally smaller type sizes.

After the patient's perform[redacted]der the above conditions is completed, tests of visi[redacted]and reading ability under

conditions of moderately dim illumination should be attempted.

An initial unfavorable response in the office, while indicative of a guarded prognosis, should not immediately rule out a more extensive trial under the usual conditions in which a patient functions.

4. Adaptation

Visually demanding situations should be avoided during the initial wearing period. A patient may at first experience some mild blurred vision, dizziness, headaches, and a feeling of slight imbalance. You should explain the adaptational symptoms to the patient. These symptoms may last for a brief minute or for several weeks. The longer these symptoms persist, the poorer the prognosis for successful adaptation.

To help in the adaptation process, the patient can be advised to first use the lenses in a comfortable familiar environment such as in the home.

Some patients feel that automobile driving performance may not be optimal during the adaptation process. This is particularly true when driving at night. Before driving a motor vehicle, it may be recommended that the patient be a passenger first to make sure that their vision is satisfactory for operating an automobile. During the first several weeks of wear (when adaptation is occurring), it may be advisable for the patient to only drive during optimal driving conditions. After adaptation and success with these activities, the patient should be able to drive under other conditions with caution.

D. Other Suggestions

The success of the monovision technique may be further improved by having the patient follow the suggestions below:

- Have a third contact lens (distance power) to use when critical distance viewing is needed.
- Have a third contact lens (near power) to use when critical near viewing is needed.
- Having supplemental spectacles to wear over the monovision contact lenses for specific visual tasks may improve the success of monovision correction. This is particularly applicable for those patients who cannot meet state driver's licensing requirements with monovision correction.
- Make use of proper [redacted] when carrying out visual tasks.

Monovision fitting success can be improved by the following suggestions:

- Reverse the distance and near eyes if a patient is having trouble adapting.
- Refine the lens powers if there is trouble with adaptation. Accurate lens power is critical for presbyopic patients.
- Emphasize the benefits of clear near vision and straight ahead and upward gaze with monovision.

The decision to fit a patient with monovision correction is most appropriately left to the Eye Care Professional in conjunction with the patient after carefully considering the patient's needs.

All patients should be supplied with a copy of the PATIENT INSTRUCTION GUIDE for these lenses. Copies are available for download at www.acuvue.com.

PATIENT MANAGEMENT

Dispensing Visit

Each sterile lens is supplied in a foil-sealed plastic package containing buffered saline solution with methyl ether cellulose. To remove the lens from the container, peel back the foil seal, place a finger on the lens, and slide the lens up the side of the bowl of the lens package until it is free of the container.

- Evaluate the physical fit and visual acuity of the lens on each eye.
- Teach the patient how to apply and remove his or her lenses.
- Explain daily disposable lens wear and schedule a follow-up examination.
- **Provide the patient with a copy of the PATIENT INSTRUCTION GUIDE for these lenses. Copies are available for download at www.acuvue.com.**

  REVIEW THESE INSTRUCTIONS WITH THE PATIENT SO THAT HE OR SHE CLEARLY UNDERSTANDS THE PRESCRIBED WEARING AND REPLACEMENT SCHEDULES.

Follow-Up Examinations

Follow-up care (necessary to ensure continued successful contact lens wear) should include routine periodic progress examinations, management of specific problems, if any, and a[redacted]h the patient of the wear schedule, daily disposable modality, and proper lens handling procedures.

Recommended Follow-up Examination Schedule (complications and specific problems should be managed on an individual patient basis):

1. One week from the initial lens dispensing to patient
2. One month post-dispensing
3. Every three to six months thereafter

NOTE: Preferably, at the follow-up visits, lenses should be worn for at least six hours.

Recommended Procedures for Follow-up Visits:

1. Solicit and record patient's symptoms, if any.
2. Measure visual acuity monocularly and binocularly at distance and near with the contact lenses.
3. Perform an over-refraction at distance and near to check for residual refractive error.
4. With the biomicroscope, judge the lens fitting characteristics (as described in the **GENERAL FITTING GUIDELINES**) and evaluate the lens surface for deposits and damage.
5. Following lens removal, examine the cornea and conjunctiva with the biomicroscope and fluorescein (unless contraindicated).
   - The presence of vertical corneal striae in the posterior central cornea and/or corneal neovascularization is indicative of excessive corneal edema.
   - The presence of corneal staining and/or limbal-conjunctival hyperemia can be indicative of an unclean lens, a reaction to solution preservatives, excessive lens wear and/or a poorly fitting lens.
   - Papillary conjunctival changes may be indicative of an unclean and/or damaged lens.
6. Periodically perform keratometry and spectacle refractions. The values should be recorded and compared to the baseline measurements.

If any observations are abnormal, use professional judgment to alleviate the problem and restore the eye to optimal conditions. If

the criteria for successful fit are not satisfied during any follow-up examinations, repeat the patient's trial fitting procedure and refit the patient.

WEARING SCHEDULE

The wearing schedule should be determined by the Eye Care Professional. Regular checkups, as determined by the Eye Care Professional, are also extremely important.

Patients tend to overwear the lenses initially. The Eye Care Professional should emphasize the importance of adhering to the initial maximum wearing schedule. Maximum wearing time should be determined by the Eye Care Professional based upon the patient's physiological eye condition, because individual response to contact lenses varies.

The maximum suggested wearing time for these lenses is:

Day	Hours
1	6-8
2	8-10
3	10-12
4	12-14
5 and after	all waking hours

REPLACEMENT SCHEDULE

These lenses are indicated for daily disposable wear and should be discarded upon removal.

LENS CARE DIRECTIONS

When lenses are prescribed for daily disposable wear, the Eye Care Professional should provide the patient with appropriate and adequate warnings and instructions for daily disposable lens wear at the time they are dispensed.

The Eye Care Professional should review with patients that no cleaning or disinfection is needed with daily disposable lenses. Patients should always dispose of lenses when they are removed and have spare lenses or spectacles available.

Basic Instructions

- Always wash, rinse, and dry hands before handling contact lenses.
- Do not use saliva or anything other than the recommended solutions for lubricating or rewetting lenses. Do not put lenses in the mouth.
- Eye Care Professionals may recommend a lubricating/rewetting solution which can be used to wet (lubricate) lenses while they are being worn to make them more comfortable.

Care for a Sticking (Non-Moving) Lens

If the lens sticks (stops moving), the patient should be instructed to apply a few drops of the recommended lubricating or rewetting solution directly to the eye and wait until the lens begins to move freely on the eye before removing it. If non-movement of the lens continues after a few minutes, the patient should immediately consult the Eye Care Professional.

EMERGENCIES

The patient should be informed that if chemicals of any kind (household products, gardening solutions, laboratory chemicals, etc.) are splashed into the eyes, the patient should: FLUSH EYES IMMEDIATELY WITH TAP WATER AND IMMEDIATELY CONTACT THE EYE CARE PROFESSIONAL OR VISIT A HOSPITAL EMERGENCY ROOM WITHOUT DELAY.

HOW SUPPLIED

Each UV-blocking sterile lens is supplied in a foil-sealed plastic package containing buffered saline solution with methyl ether cellulose. The plastic package is marked with the following:

- ACUVUE OASYS® 1-Day: base curve, power, diameter, lot number, and expiration date
- ACUVUE OASYS® 1-Day [redacted]MATISM: base curve, power, diameter, cylinder, axis, lot number, and expiration date

REPORTING OF ADVERSE REACTIONS

All serious adverse experiences and adverse reactions observed in patients wearing these lenses or experienced with these lenses should be reported to:

Johnson & Johnson Vision Care, Inc.
7500 Centurion Parkway
Jacksonville, FL 32256
USA
Tel: 1-800-843-2020
www.acuvue.com

Johnson & Johnson Vision Care, Inc.
7500 Centurion Parkway
Jacksonville, FL 32256
USA
Tel: 1-800-843-2020
www.acuvue.com

20401080

In Canada: Johnson & Johnson Vision Care, division of Johnson & Johnson, Inc.
In USA: Johnson & Johnson Vision Care, Inc.
Printed in USA.
Revision date: 09/16
Revision number: AO-03-16-13

APPENDIX D: CLINICAL TECHNICAL PROCEDURES [redacted]

[redacted] Determination of Near Addition
[redacted] Lens Fitting Characteristics
[redacted] Subject Reported Ocular Symptoms/Problems
[redacted] Front and Back Surface Lens Deposit Grading Procedure
[redacted] Determination of Distance Spherocylindrical Refractions
[redacted] Biomicroscopy Scale
[redacted] Conjunctival Staining
[redacted] Keratometry Procedure
[redacted] Distance and Near Visual Acuity Evaluation
[redacted] Distance LogMAR Visual Acuity Measurement Procedure
[redacted] Patient Reported Outcomes
[redacted] Lens Insertion and Removal
[redacted] White Light Lens Surface Wettability
[redacted] Visual Acuity Chart Luminance and Room Illumination Testing

[redacted] DETERMINATION OF NEAR ADDITION

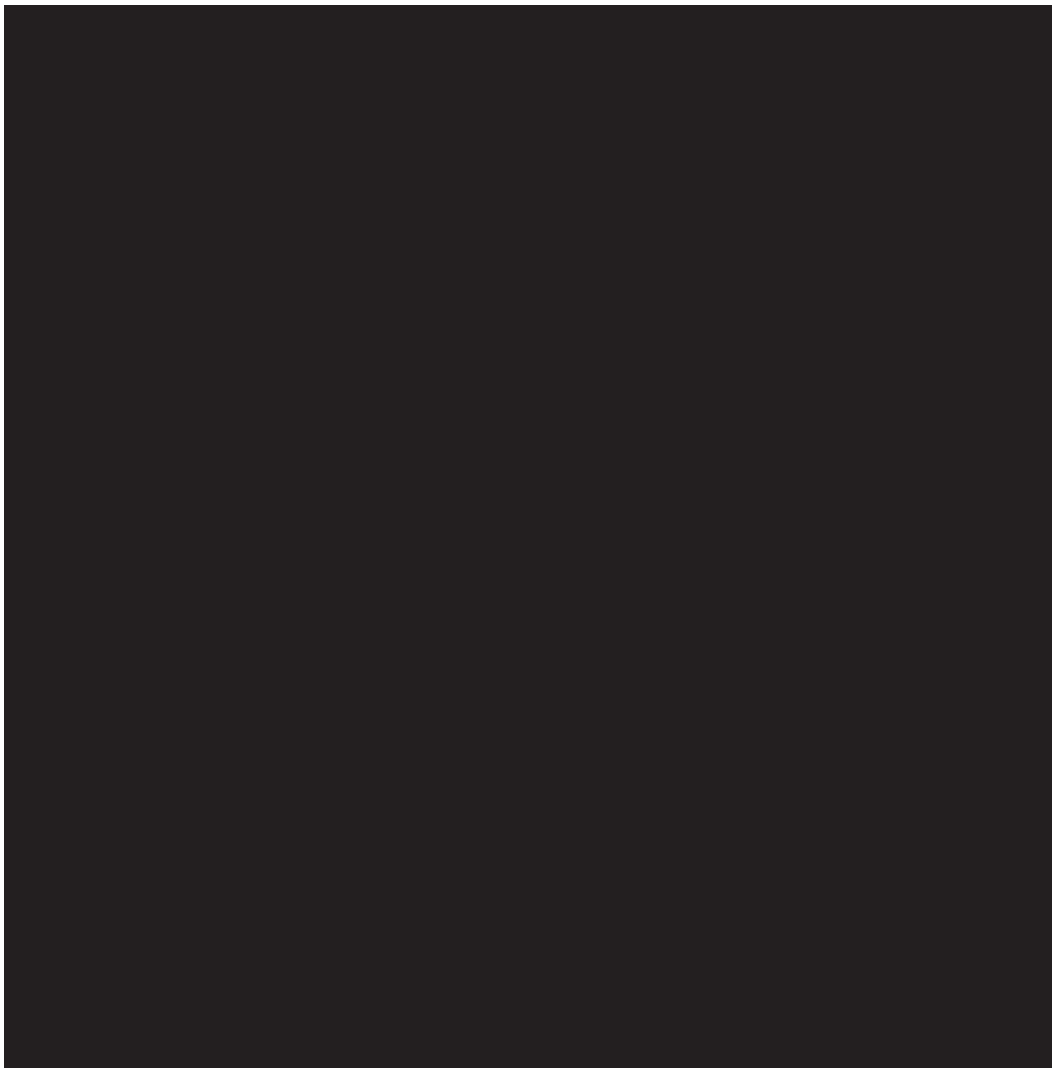
[redacted] **Determination of Near Addition**

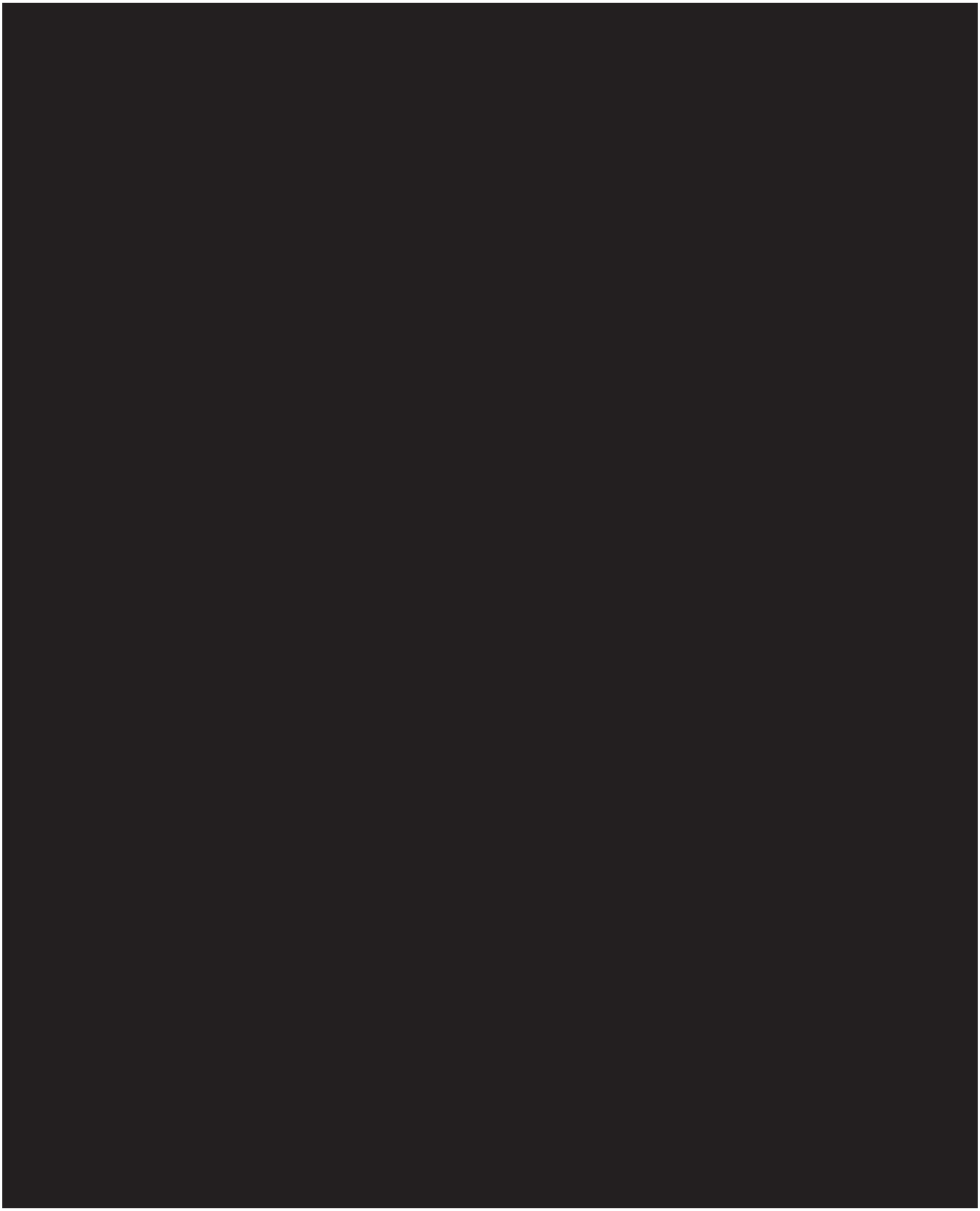
[redacted]

[redacted]

[redacted]

[redacted]





[redacted] LENS FITTING CHARACTERISTICS

[redacted] Lens Fitting Characteristics

[redacted] [redacted]

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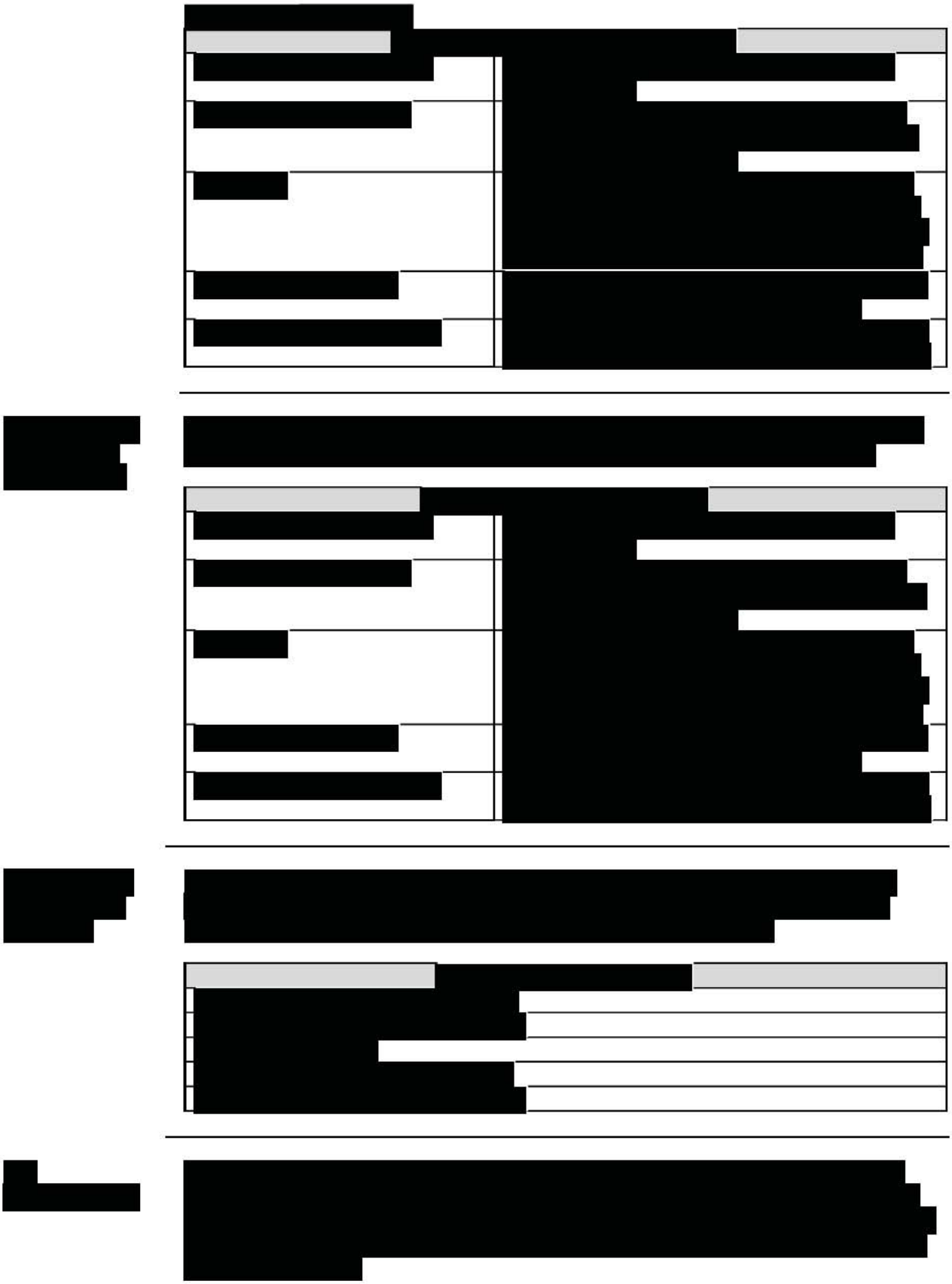

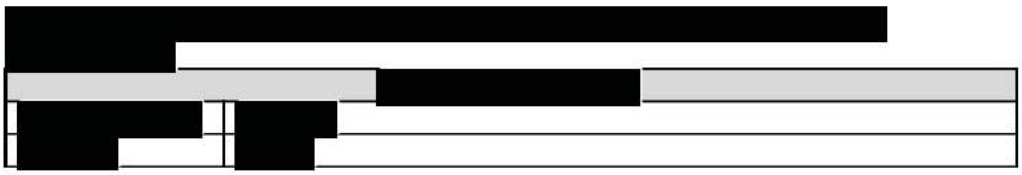

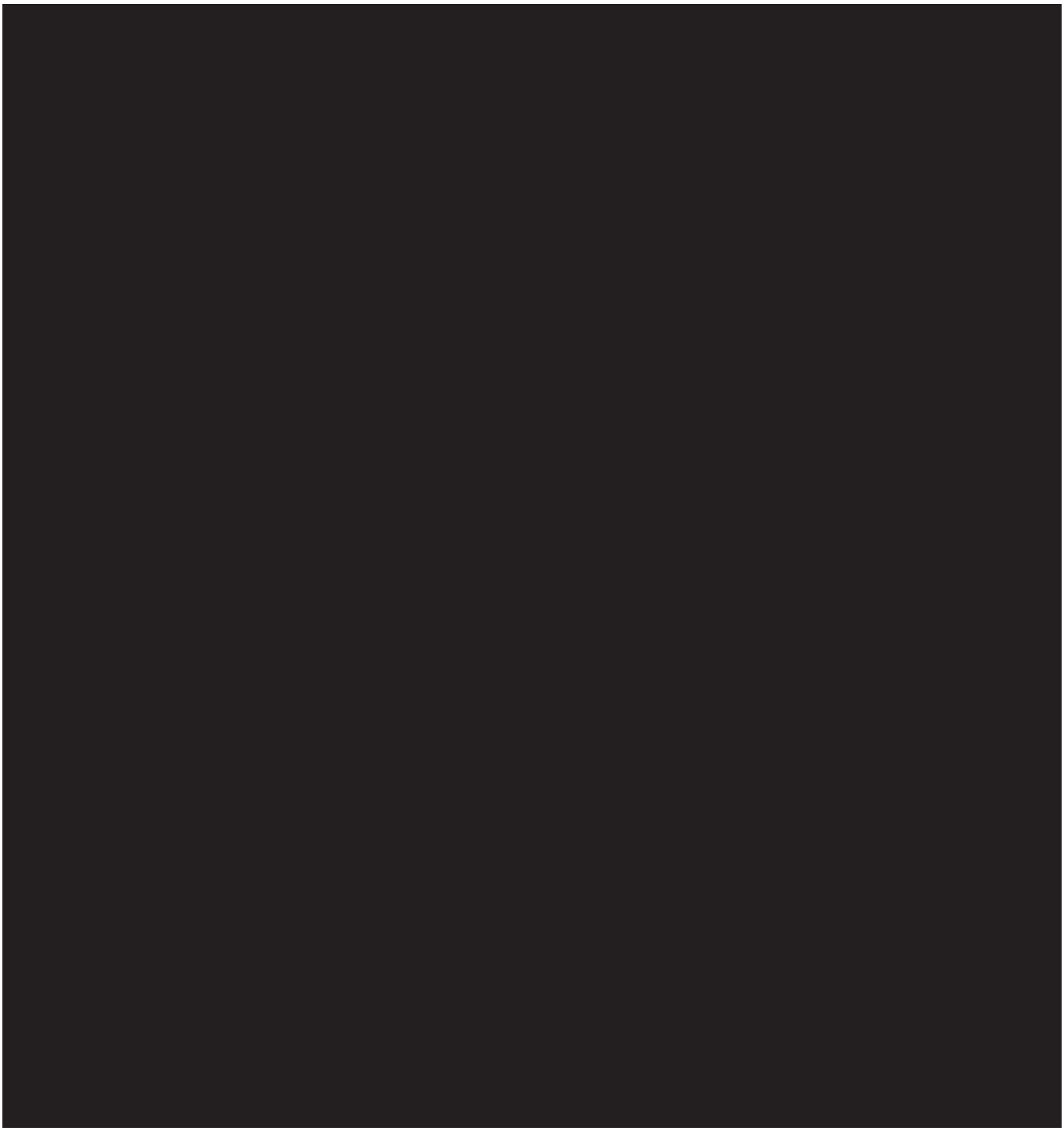

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Front and Back Surface Lens Deposit Grading Procedure

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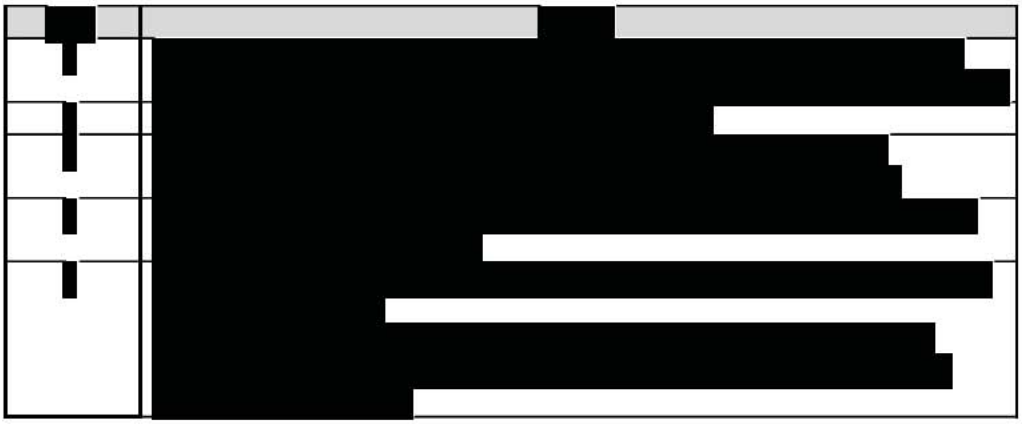

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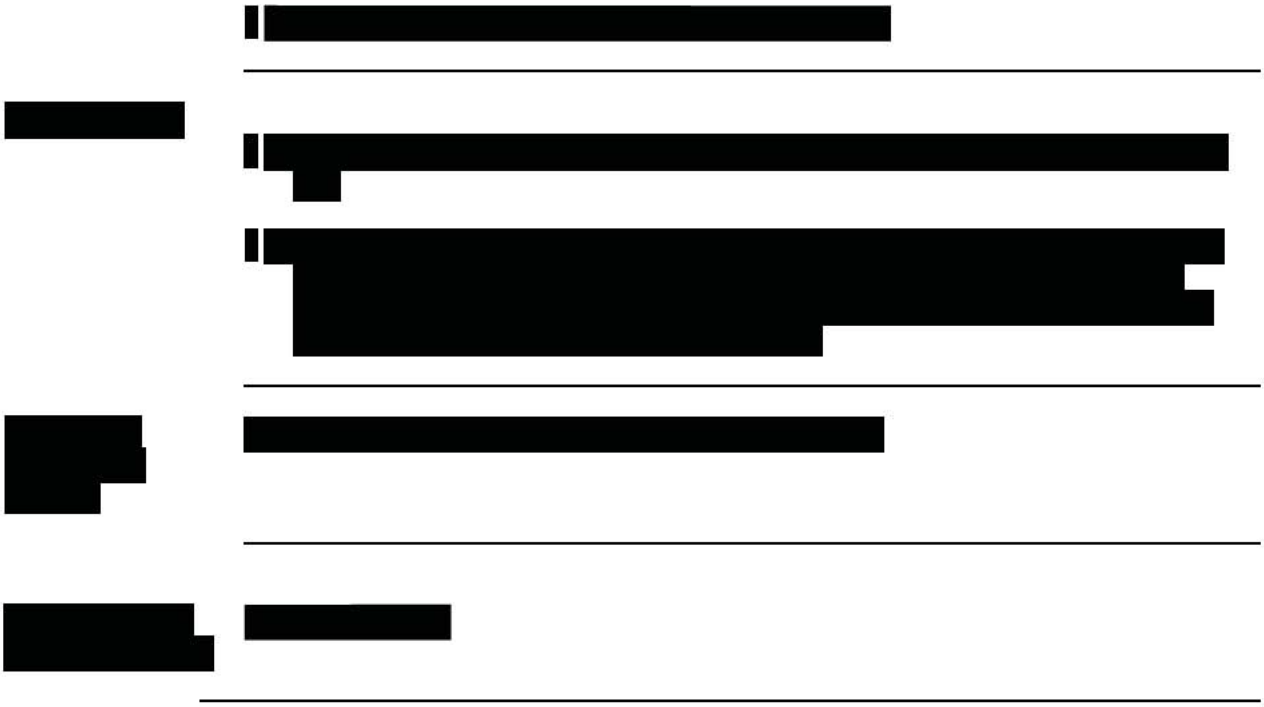

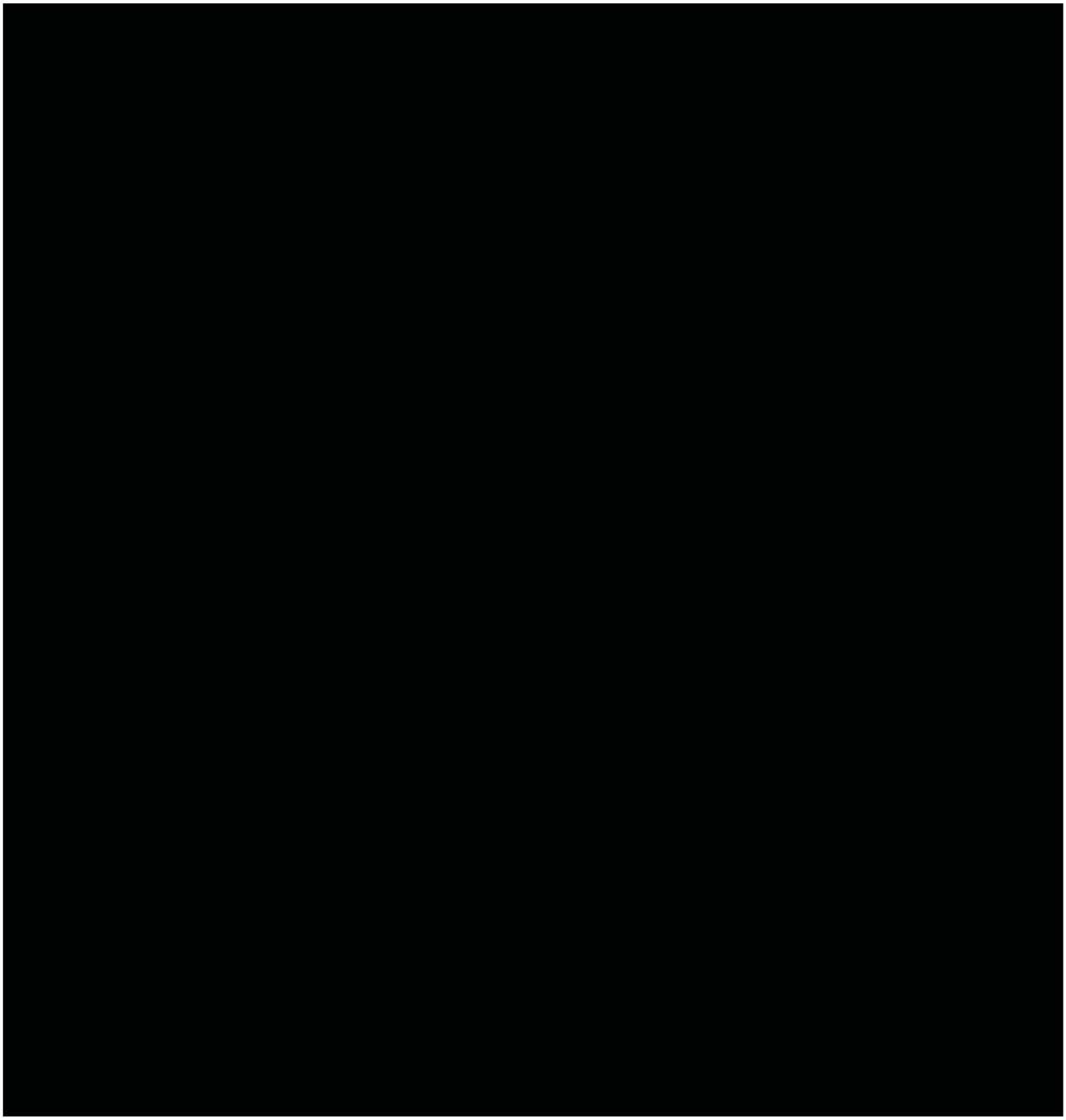

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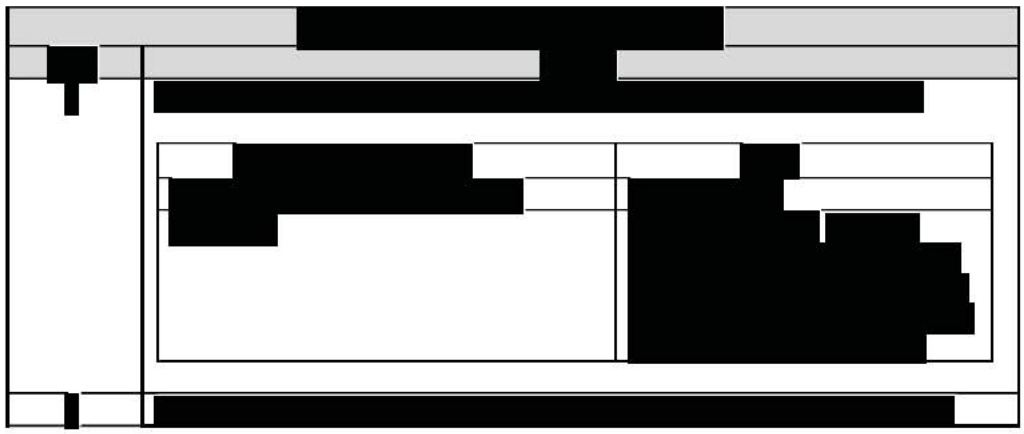

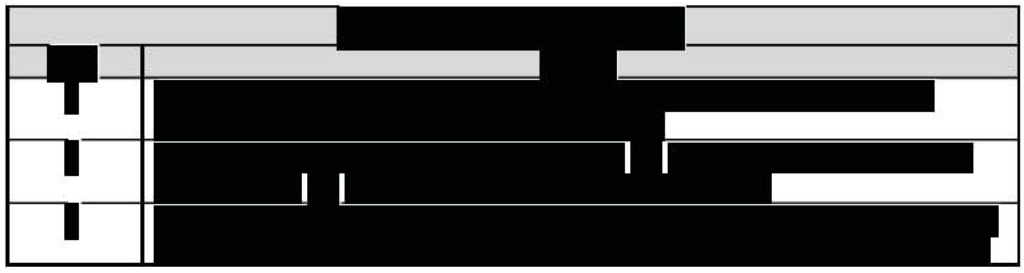

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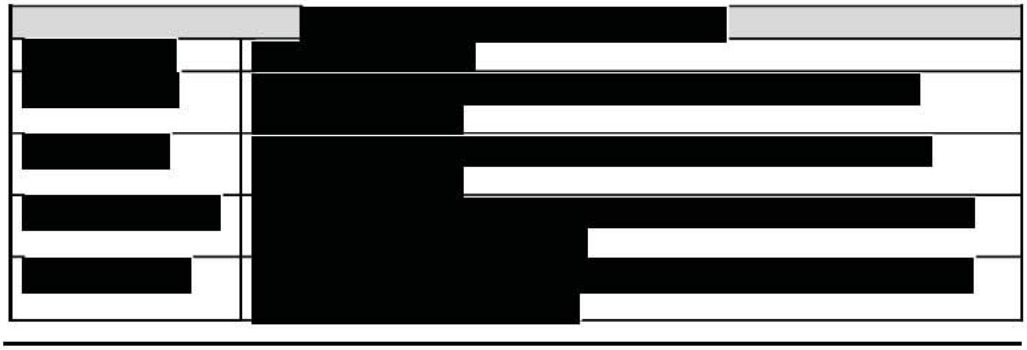

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[redacted] KERATOMETRY PROCEDURE

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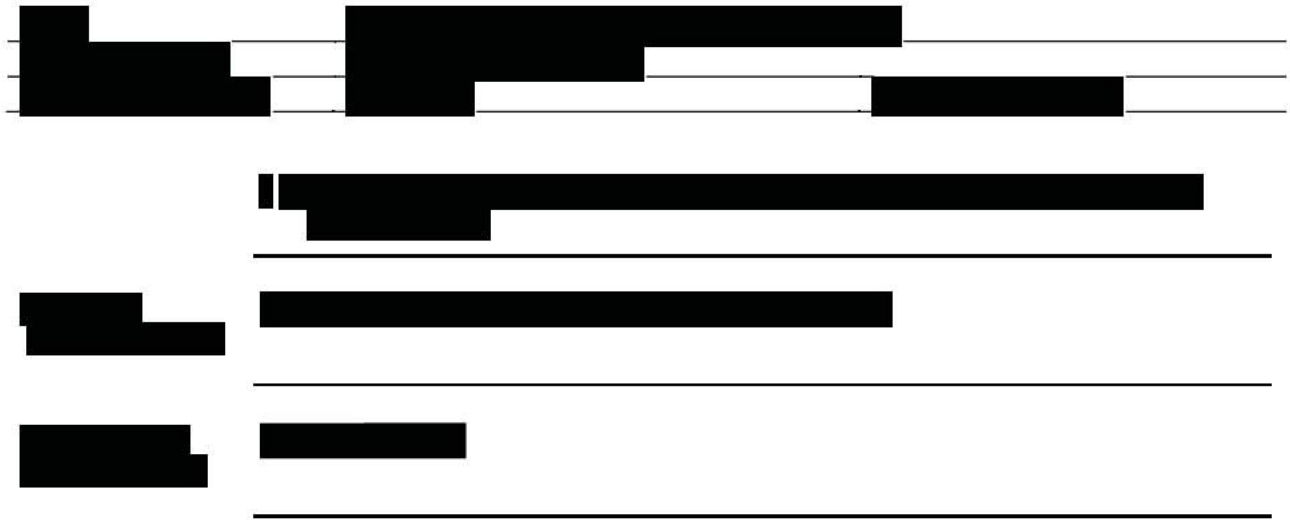

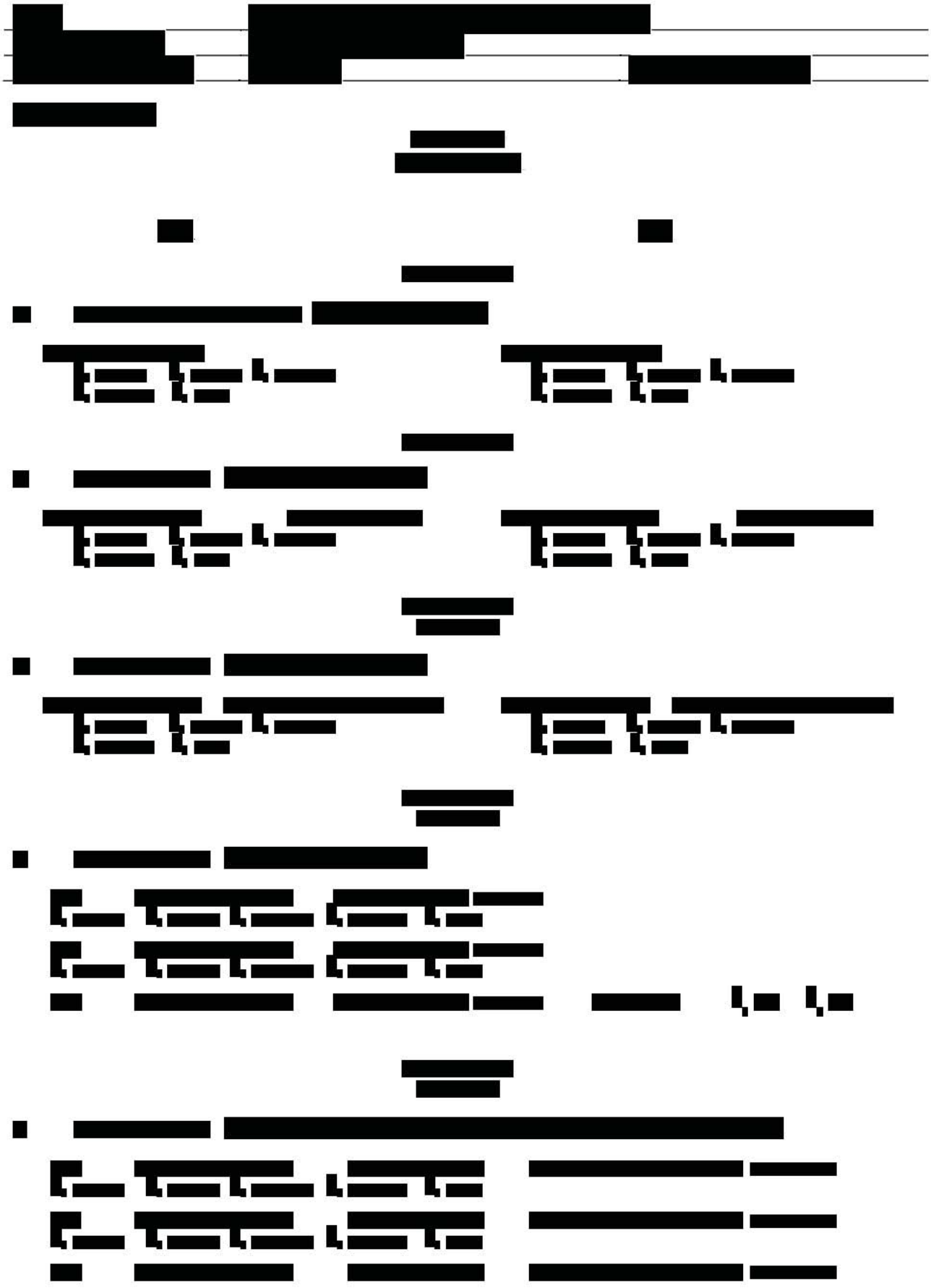

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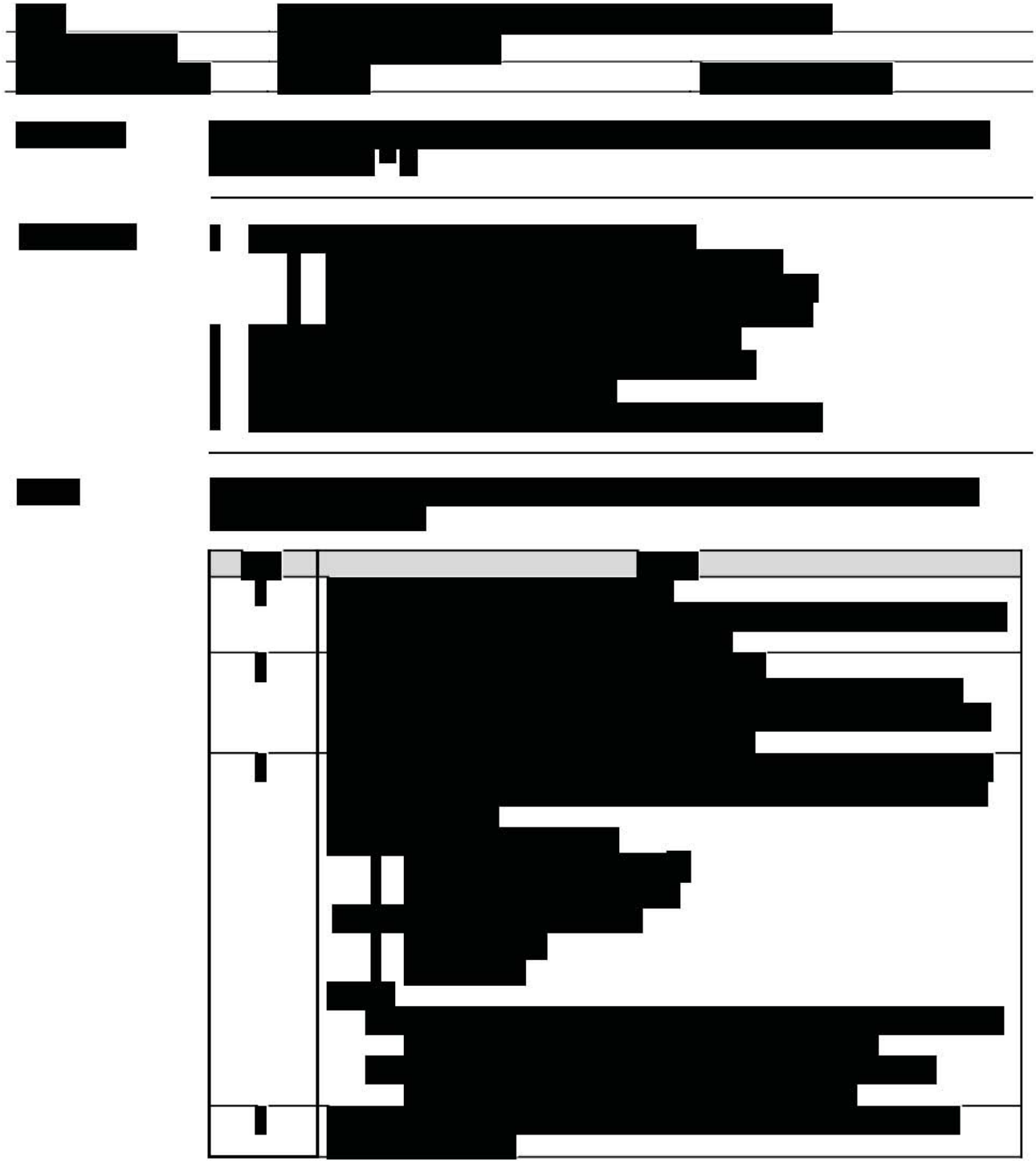

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White Light Lens Surface Wettability

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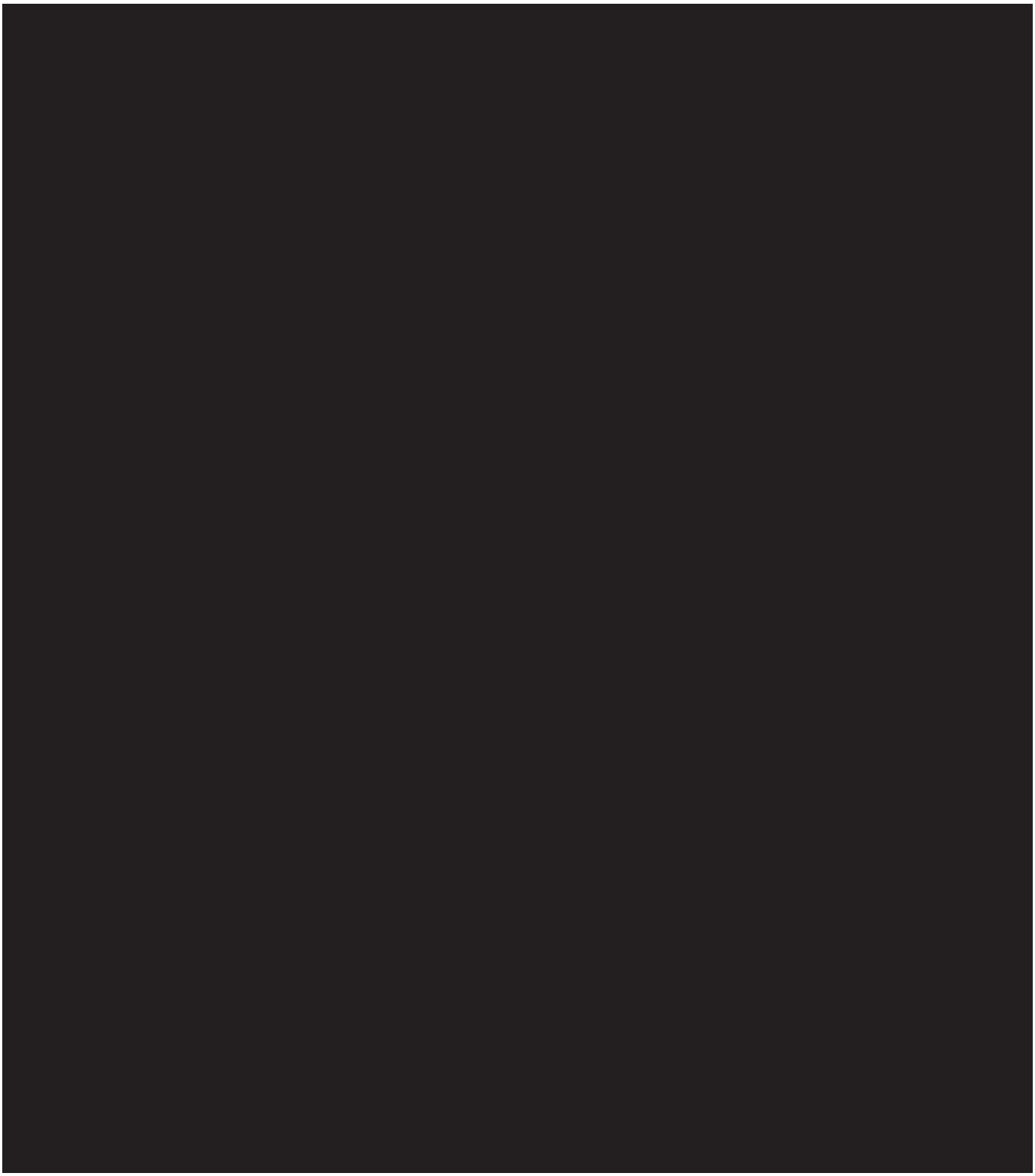

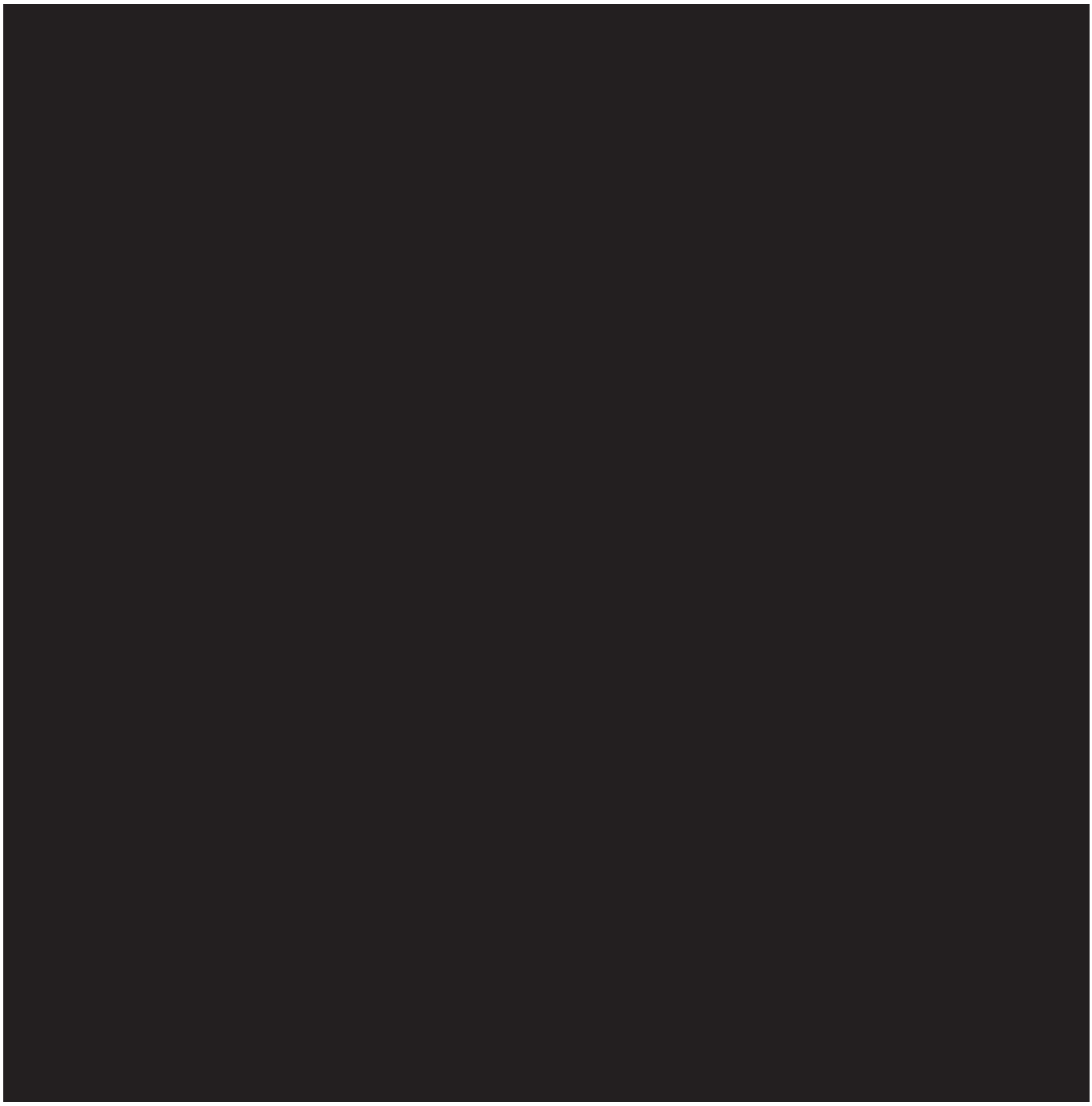

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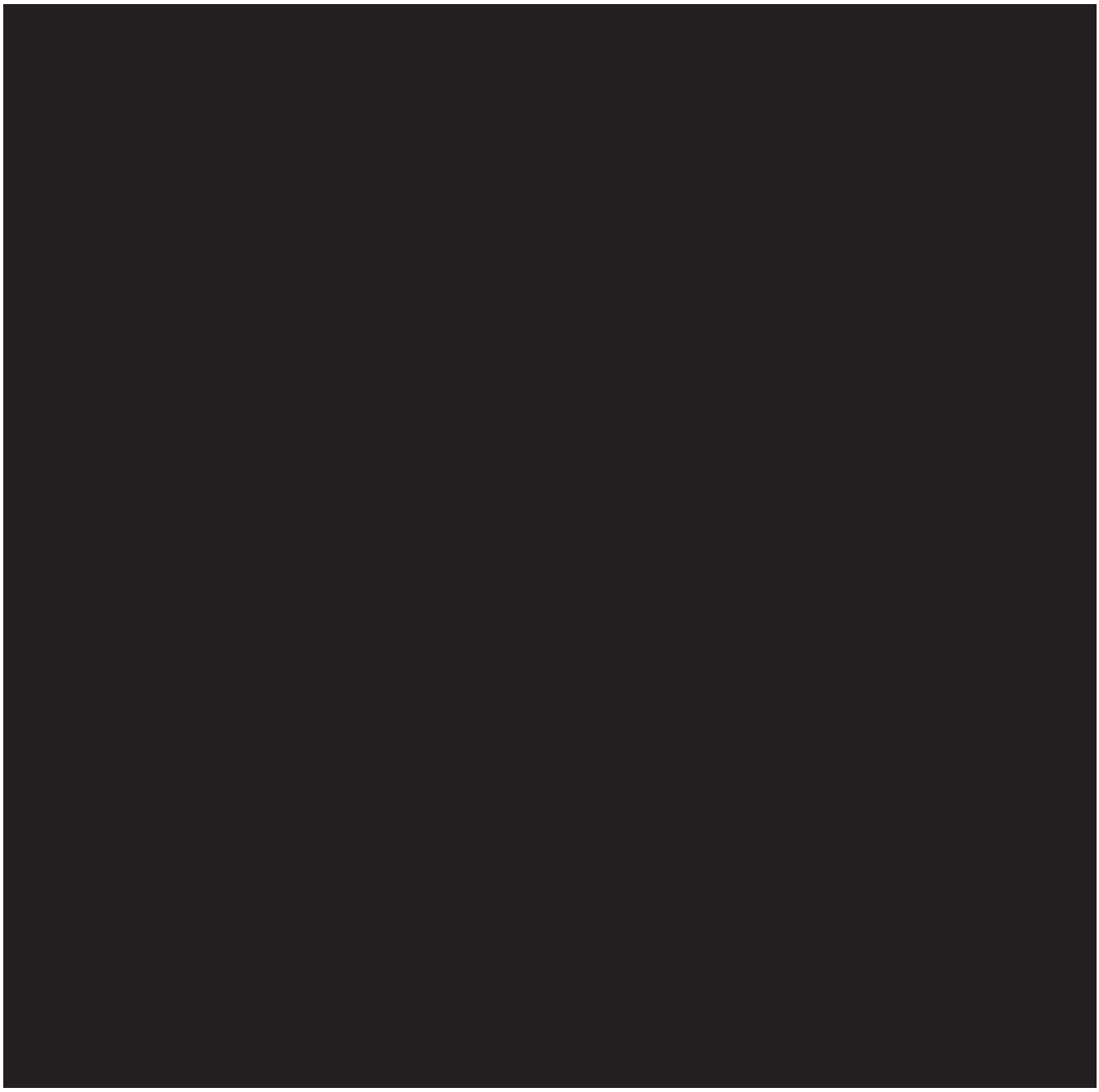
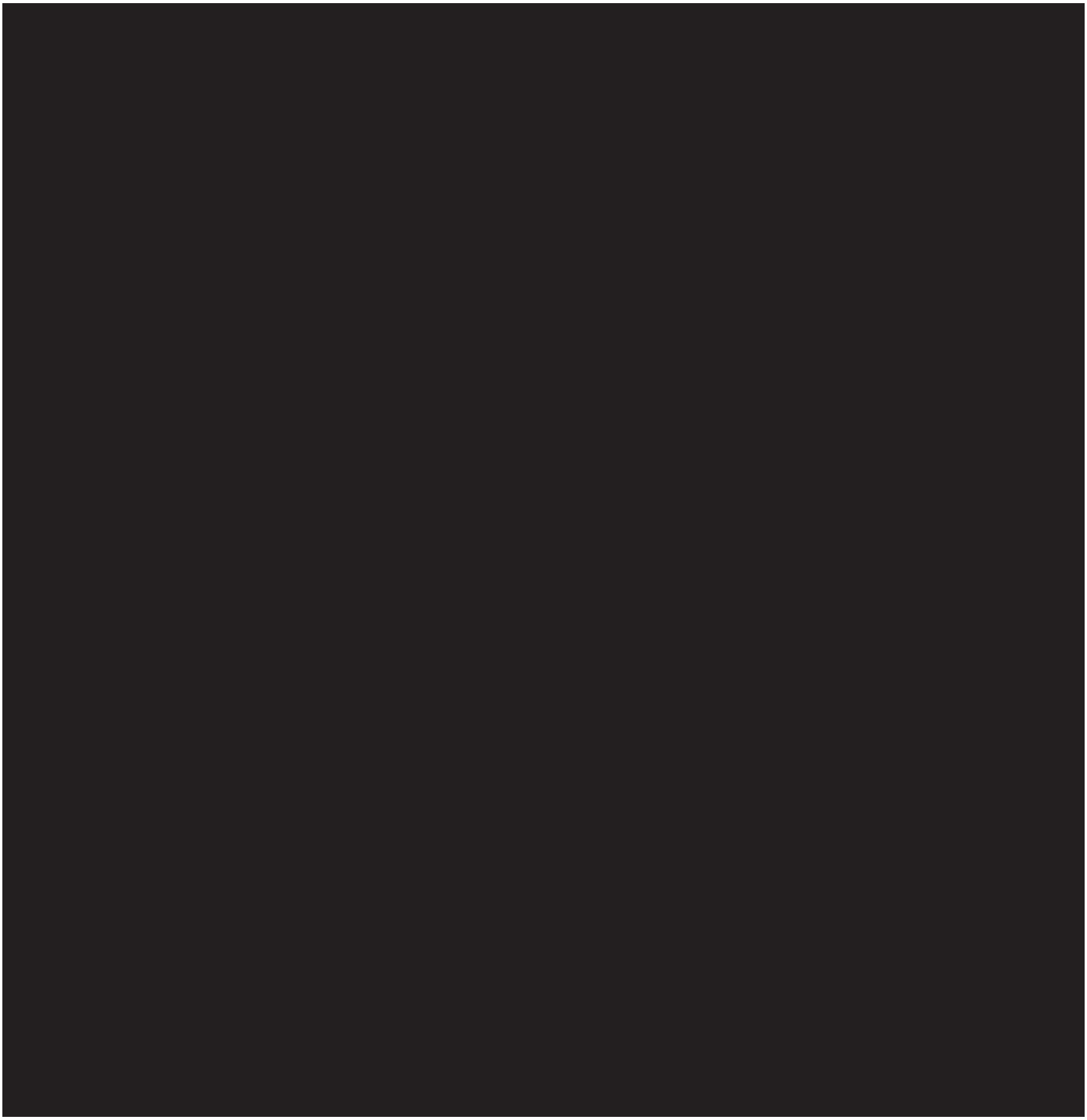




APPENDIX E: NON-INVASIVE BREAK-UP TIME (NIBUT) WORK AID

WORK AID: NON-INVASIVE TEAR BREAK-UP TIME (NIBUT) MEASUREMENT USING THE MEDMONT E300 CORNEAL TOPOGRAPHER

1.0 OBJECTIVES

Tear break-up time is a standard clinical measurement used to indicate the stability of the pre-ocular tear film. An individual with an unstable tear film can experience symptoms of visual disturbances or discomfort. The Medmont videokeratoscope is one type of instrument which may be used to view the regularity of the tear film, since it displays a live video image of a set of illuminated rings reflected by the eye surface. Disturbances to the tear film can be visualized as disruptions to the reflected ring pattern. This measurement is a form of non-invasive tear break-up time (NIBUT), since the instrument does not touch the eye and there is no use of topical dyes.

2.0 MATERIALS

The Medmont E300 Corneal Topographer is a computerized videokeratometer which uses Placido rings to map the surface of the human cornea.

SOFTWARE VERSION

The E300 Software is part of the Medmont Studio integrated software environment. The instructions in this Appendix apply to Medmont Studio 4 software *version 4.14.1.* Other versions of the software are unlikely to have substantial difference in basic function or data integrity.

3.0 DATA MANAGEMENT

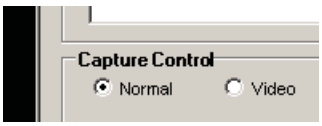
The Medmont videokeratoscope consists of a light source made up of a series of concentric rings, and a video camera for recording the reflected image of these rings. For tear break-up time measurement, it is not necessary to save the series of images, but this may be done as an optional step for proof of performance or if needed for further analysis. Tear break-up time is measured with a stopwatch and the results are recorded on paper CRF forms or an eCRF data entry screen.

4.0 PROCEDURES

MEDMONT SOFTWARE SETUP

If videokeratoscope images are not being saved, it is not necessary to enter a new patient name or date of birth. Selecting video data collection mode will ensure that a continuous live video view of the participant's eye is shown on the computer monitor.

Figure 1. Selecting Normal (single frames) or Video capture control

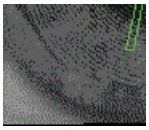


PARTICIPANT SETUP

While instrument and participant alignment is being set up, the participant should be instructed to continue blinking normally.

The patient should sit comfortably in the chair. Ask the participant to put their chin onto the chinrest and put their forehead firmly against the forehead rest. Adjust the chinrest height until the eye is approximately level with the mark on the vertical bar of the headrest. The participant should push their chin forward slightly on the chinrest. Ask the participant to look into the centre of the green central illuminated ring and keep their gaze on this target during the measurement. The investigator will use the instrument joystick to move the instrument to the correct distance from the eye, and to align the instrument axis (shown as a green cross overlay) with the reflection of the central reflected ring. A red line indicates whether the instrument is too close or too far away from the participant's eye.

Figure 2: Focus examples showing Too Far, In Focus, and Too Near



If it is not possible to move the instrument in to best focus due to obstruction by the eyebrow, instruct the participant to move their chin slightly further forward on the chinrest, or their forehead slightly back from the headrest. If the instrument is obstructed by the side of the nose, ask the participant to turn their head so that their nose moves further away from the instrument.

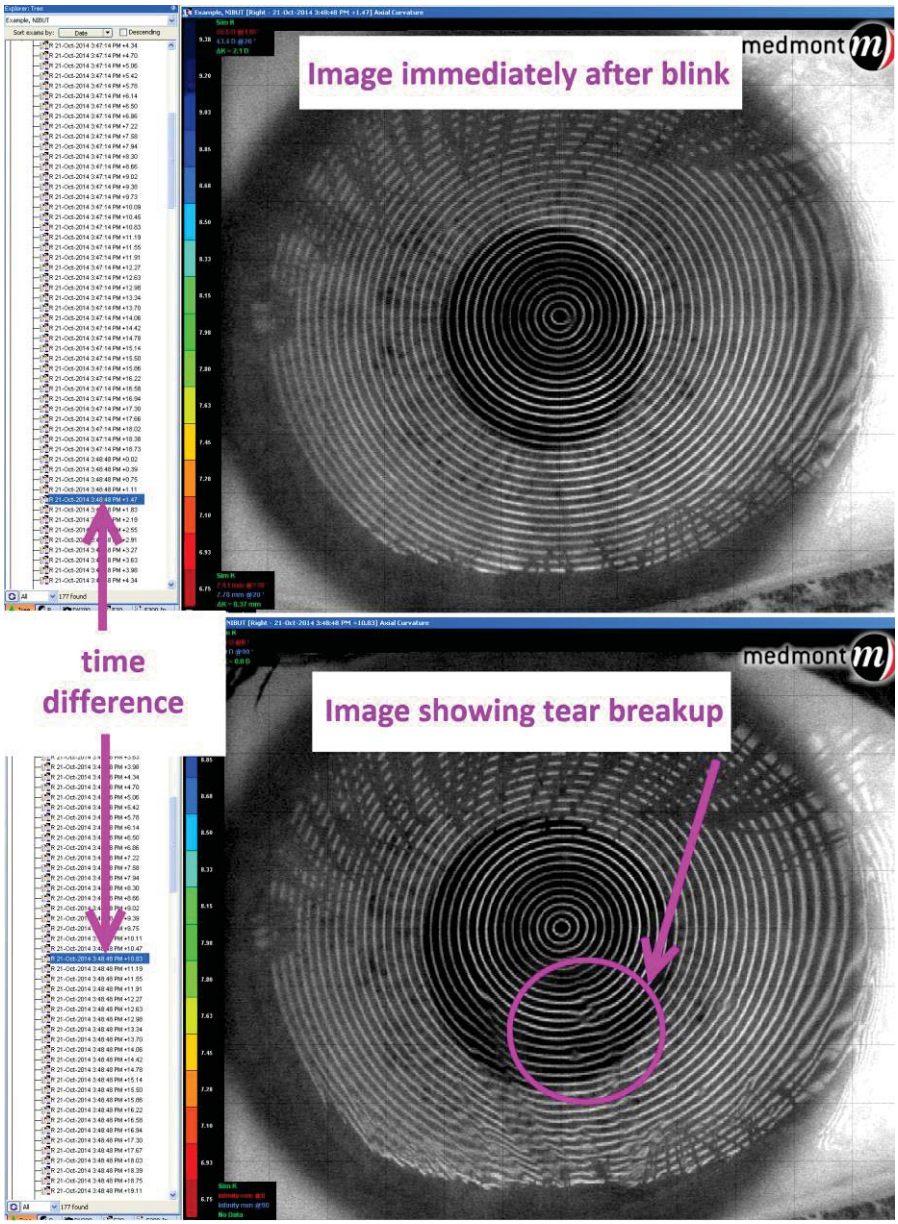
MEASURING TEAR BREAK-UP TIME

When the examiner is ready to commence the measurement, the participant is instructed to have a final blink (the blink should be natural, not forceful) and then to stop blinking for as long as possible and continue to look straight ahead at the central green ring. NIBUT is measured as the time interval in seconds after the final blink to the first appearance of distortion in the reflected

rings; or to the time that the participant has to blink due to discomfort. The investigator must watch for a change in the appearance of the ring pattern compared to the immediate post-blink appearance. Events that are considered distortions and thus endpoints include: debris that causes a break in the grid pattern, localized bending or blurring of a section of the ring pattern, or a distinct doubling of any lines.

The standard measurement of tear film break-up time involves three measurements on each eye. Between measurements, ask the participant to sit back from the chinrest for at least 30 seconds and to blink naturally. Taking measurements too rapidly without a sufficient rest period can result in a gradually worsening (ie. decreasing) tear film break-up time.

Figure 3: An example of the appearance of tear breakup



SAVING THE SERIES OF IMAGES (OPTIONAL)

The raw images may be saved using "***File/Save All Images***".

In order to also save the series of topography maps, click on "***File/Analyze All***" before "***File/Save All Images***".

5.0 PHOTODOCUMENTATION

Not applicable

6.0 ADDITIONAL INFORMATION

Not applicable

7.0 TRAINING REQUIREMENTS

Read only

8.0 CASE REPORT FORM MODULE

The standard Bioclinica eCRF screen will record three measurements of NIBUT (in seconds) for each eye.

DOCUMENT CHANGE HISTORY

Originator	Change Description	Effective Date
R. Franklin	New specification.	October 21, 2014

APPENDIX F: NON-INVASIVE KERATOGRAPHIC BREAK-UP TIME (NIKBUT) WORK AID

WORK AID: Measurement of non-invasive tear break up time and tear meniscus height with the Oculus Keratograph 5M

1.0 OBJECTIVES

Perform two types of assessment of tear film quality using the Oculus Keratograph 5M instrument. Non-invasive keratographic tear break up time (NIKBUT) is an objective way of detecting the time period after a blink at which the tear film begins to become unstable, and the location of that instability. Tear meniscus height is a measurement which is used to express the relative quantity of tears present in the eye. Other functions of the Keratograph instrument such as corneal topography, meibography and ocular redness are not covered in this document.

2.0 MATERIALS

The Oculus Keratograph 5M multifunction diagnostic instrument is a clinical device manufactured by Oculus (Germany).

SOFTWARE VERSION

The instructions in this Appendix apply to software version 6.08r25 for patient data management. Other versions of the software are unlikely to have substantial difference in basic function or data integrity.

3.0 DATA MANAGEMENT

The Oculus Keratograph 5M software generates computer files which are considered source data. At a minimum, the Source Data must be saved in a secure location and a backup copy created at the end of each study.

Primary source data are the image files, video files and the Oculus Keratograph 5M internal database. Secondary source data are output data files (.csv), still image files (.jpg, .png or .bmp), video files (.mkv) and any on-screen data which are transferred to a paper or electronic Case Report Form. Tertiary source data are output data that has been transferred to an Excel sheet for further analysis.

4.0 PROCEDURES

CALIBRATION

The instrument does not require recalibration on site.

ROOM SETUP

Perform the examination in a dim or darkened room, and ensure that the area is free from sources of light which may reflect from the participant's eye to the instrument.

PATIENT SELECTION

The recommended practice is to enter patient information before starting to capture and analyze an exam. On the Home Screen (Figure 1), select the icon (indicated as number 1) to add a new patient. In a clinical trial, use the Last Name field to record the study name and subject number (eg. CR6285-007), use the First Name field to record the visit number and condition (eg. V1-Bare) and use the Dat. o. B. field to record the date of the examination.

Figure 1: Oculus Keratograph 5M Home Screen

After entering in the Patient Information, choose "Keratograph" (shown as 2 above) to go to the Examination screen. To create a new examination, select "Examination" from the tool bar (indicated by number 1 in Figure 2). A drop down will appear, select "New."

SELECTING MEASUREMENT TYPE

Once on the Examination screen, the type of measurement may be selected from the list of available tests under TF-Scan:

- **Tear Meniscus Height:** (indicated as number 2 in the figure below)
- **NIKBUT:** (indicated as number 3 in the figure below)

Figure 2: Examination Screen

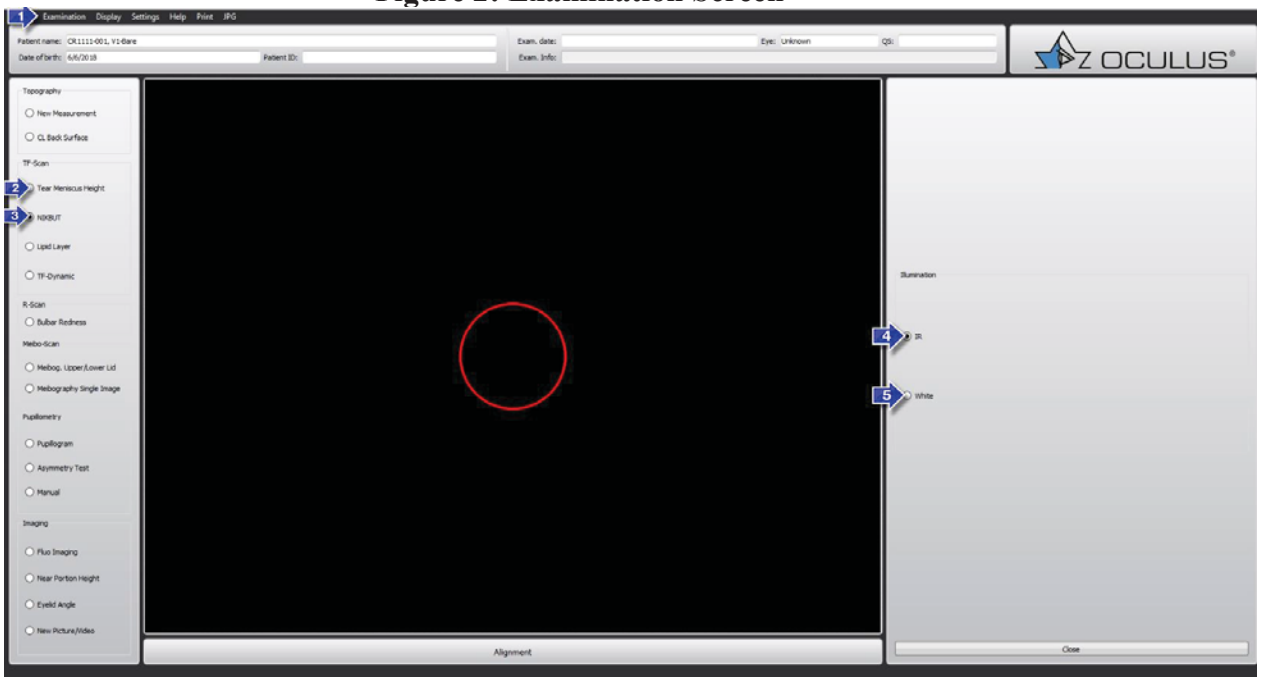
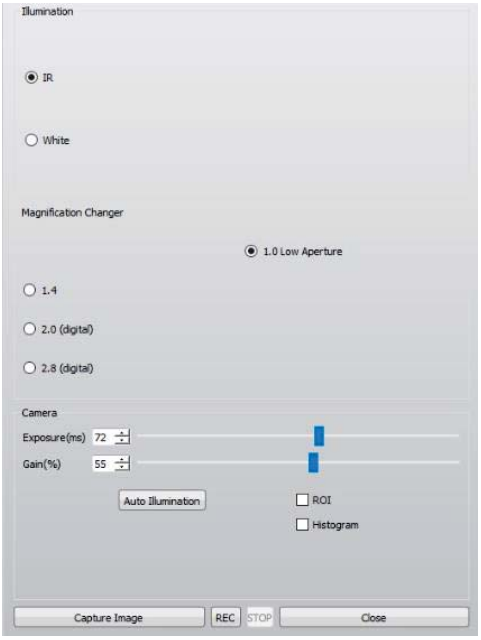


Figure 3: Tear Meniscus Height Illumination Screen



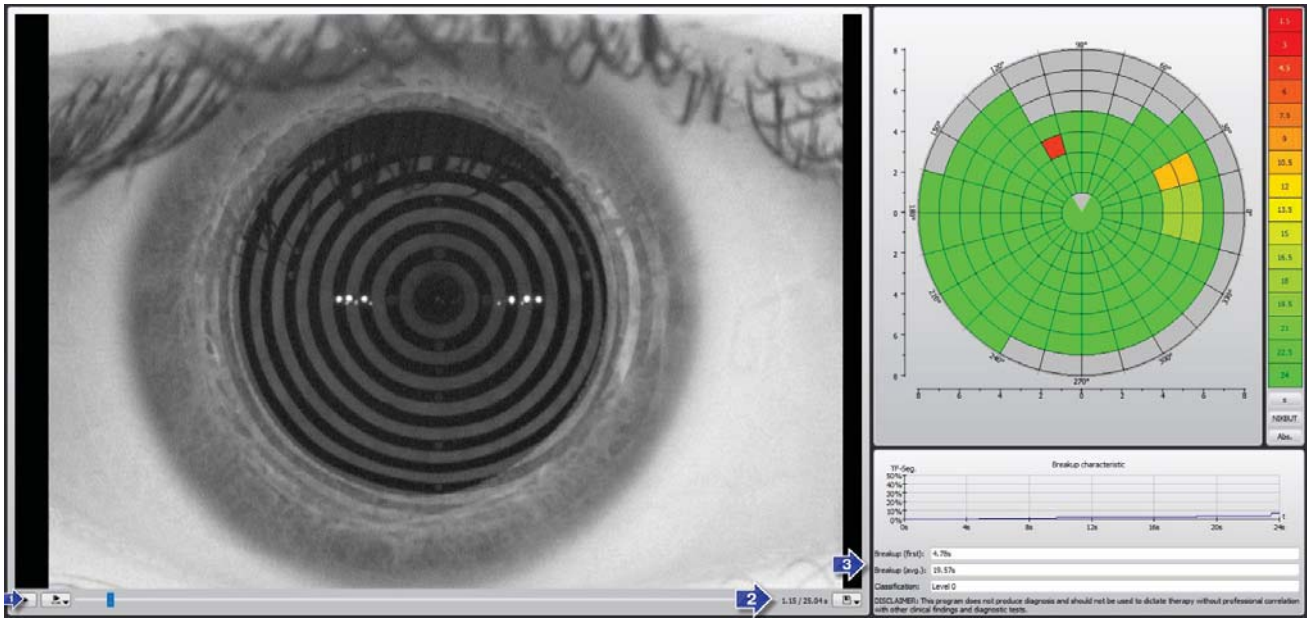
MEASUREMENT PROCEDURE

The patient should sit comfortably in the chair. Ask the patient to put their chin onto the chinrest and put their forehead firmly against the forehead rest. Ask the patient to look at the center of the fixation target and keep their gaze on this target. For the NIKBUT test, the target will be a red light. For tear meniscus height, there will not be a target, so instruct the patient to look straight ahead and maintain their gaze.

NIKBUT

After selecting NIKBUT from the test menu, a red cross should appear in the center of the red ring that will be bordered by four bars when aligned. Select "IR" lighting in the Illumination box on the right side of the screen (indicated as number 4 in Figure 2). Adjust the camera to the proper focus. The screen will prompt which corrections need to be made to reach the proper orientation. Once aligned and focused there will be a prompt to instruct the patient to blink 2 times. Ask the patient to complete 2 full blinks and then hold their eye open as wide as they can for as long as they can. The instrument will start recording automatically and will stop when the patient blinks, or when there is extreme tear break up, or after 25 seconds. After conducting a NIKBUT test, allow approximately 2 minutes for tear film recovery time before attempting another measurement. If the patient accidentally blinks too early or moves causing an incomplete scan, wait approximately 2 minutes before repeating the test. Remind the patient to try to hold open their eye for as long as they can.

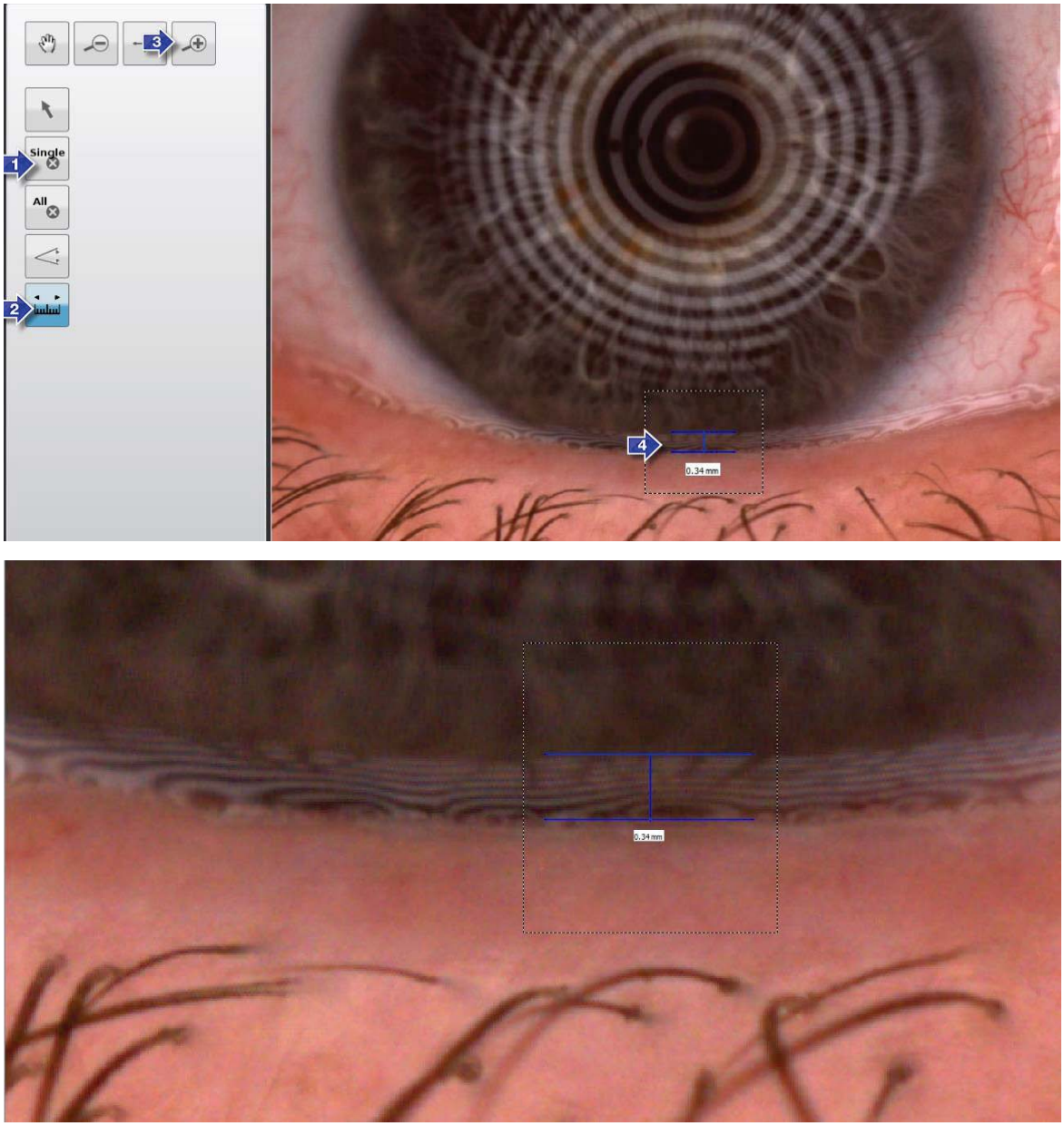
Figure 4. Completed NIKBUT Examination



Tear Meniscus Height Image Capture

After selecting Tear Meniscus Height from the test menu, select 1.0 zoom and "White" lighting in the Illumination box on the right side of the screen. Adjust the camera focus so that the lower lid tear meniscus is more centrally displayed than it was during the NIKBUT test. Adjust the instrument until the tear meniscus is in best focus. Then instruct the patient to blink. At approximately 2 seconds after the blink, either select "Image" to capture the picture on the screen or press down on the foot pedal. A still image will be captured. Multiple images may be collected as specified in the study protocol.

Figure 5: Complete Tear Meniscus Height Examination



Measuring Tear Meniscus Height on a captured image

Once the image is taken, a new screen will appear. Measurement of tear meniscus height may be performed now, or the image may be reloaded at a later time for analysis. The meniscus height will be measured at the point of the tear film that is straight down from the center of the pupil. To begin a measurement, use the icon indicated by number 3 in Figure 4 to zoom in on the tear film, press the icon 6 times for the proper amount of zoom. Next, select the icon indicated by number 2 in Figure 4. Click on the upper most part of the tear meniscus, then click where the eyelid margin meets the eye. This will

create a blue marker and provide a numerical measurement of tear meniscus height. If the measurement is not aligned or an error occurred, the icon indicated by number 1 in Figure 4 will delete the measurement. The measurements save to the computer automatically.

EXPORTING THE NIKBUT DATA

Under Patient List select the patient the data is needed for. Choose "Export" towards the bottom of the screen. On the Export patient data window, select "Folder" (indicated as number 1 in Figure 6) and then select the "…" (indicated as number 2 in Figure 6). A Browse for folder window will open, the proper folder can be found under This PC (number 1 in Figure 7) then Windows (C:) (number 2 in Figure 7). Choose the TOPO folder (number 3 in Figure 7) then the study-specific folder (number 4 in Figure 7). Select OK to finish selecting the export location. The window will close, select Export (indicated as number 3 in Figure 6) to save the data in the trial folder. The data may then be copied to a USB data drive for transfer to another computer and opened in Excel for further analysis.

Figure 6. Export Patient Data Window

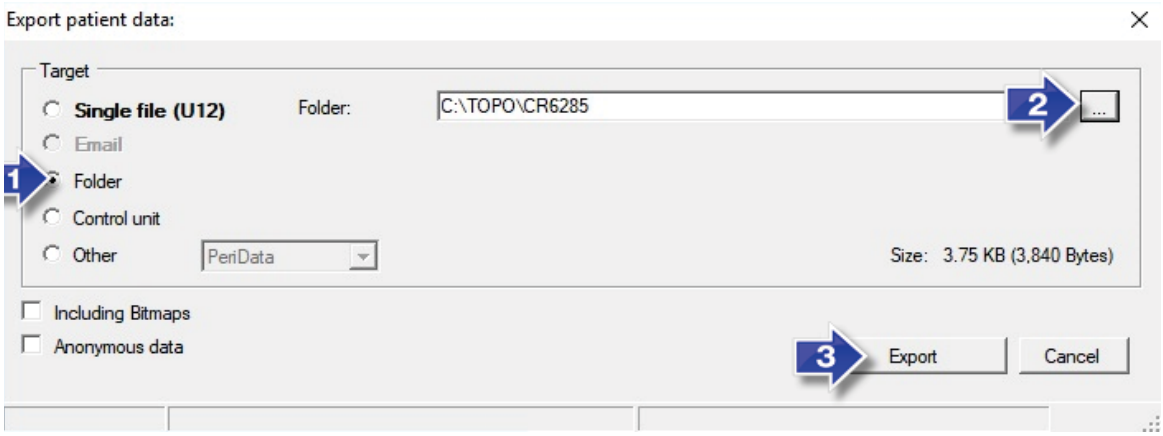
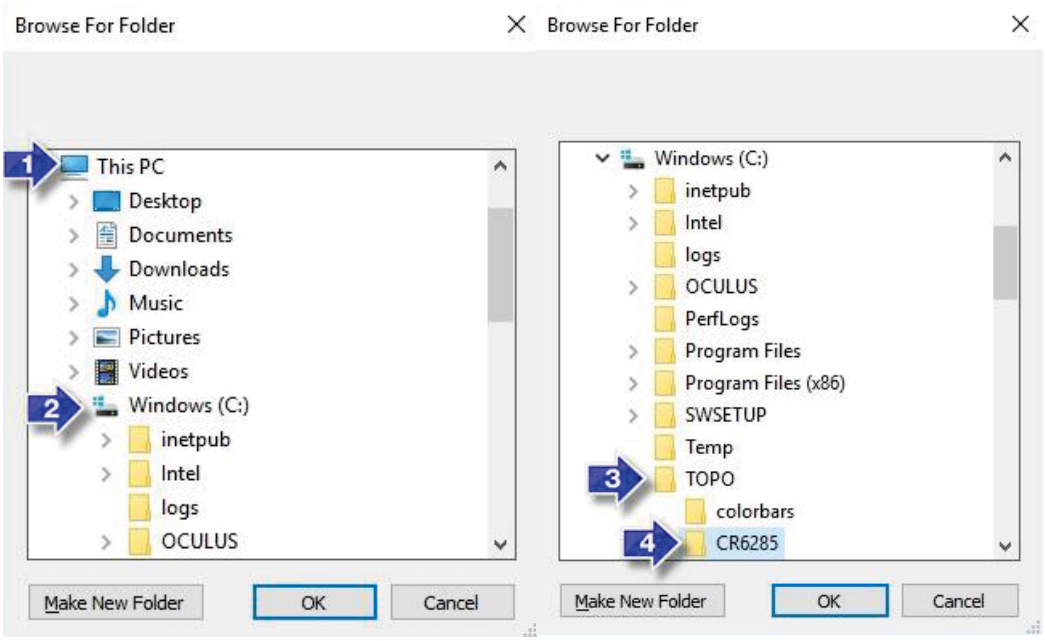


Figure 7. Browse for Folder Window



5.0 PHOTODOCUMENTATION

Not applicable

6.0 ADDITIONAL INFORMATION

Additional information may be found in the user manual for the instrument.

7.0 TRAINING REQUIREMENTS

Read only

8.0 CASE REPORT FORM MODULE

A number of different Bioclinica forms will be required for the recording of different types of data, depending on the needs of the study.

APPENDIX G: LIPIVIEW II MANUFACTURER INSTRUCTIONS

TearScience®

LipiView® II

Ocular Surface Interferometer

Instructions for Use

Model LVI-2000

running Software Version 3.X

Manufactured by:

TearScience, Inc.
5151 McCrimmon Parkway Suite 250
Morrisville, NC 27560
Phone: (919) 467-4007
Fax: (919) 467-3300

EC REP
Donawa Lifescience Consulting
Piazza Albania, 10
00153 Rome, Italy

Rx only

CE
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Revision History			
Revision	**Date**	**Description of Changes**	**ECR # or PCR #**
A	19 Nov 2014	Initial release of Instructions for Use for LipiView II/3.x software.	P1407211
B	31 July 2015	Made updates for software version 3.11. Replaced Figure 6. Fixed minor typographical and formatting errors.	P1502121
C	1 February 2016	Previous revisions of this document were numbered 012051-ENG. To accommodate the release of varied English versions, this document is now numbered as 012051-US with the following applicable changes: Removed phrase "All of these image types can be photographically documented and visually monitored" from Indications for Use. Removed information pertaining to Model LVI-1001. Updated phototoxicity warning with ISO 15004-2 required information. Clarified patient contact components and added disinfection of Lid Everter to Device Description and Warning sections (already described in Cleaning and Instructions sections of the manual). Added inspection of Lid Everter to Device Description and Instructions. Added USB mouse and keyboard to Accessory Support. Updated recording time from 10 to 5 seconds in Capture Ocular Images procedure. Updated document copyright date to 2016.	P1601281

Contents

Figures

Tables

1 Introduction

This manual provides the indications, contraindications, warnings, precautions, potential adverse effects and instructions for use for the *TearScience®* LipiView® II Ocular Surface Interferometer. **Carefully read this manual in its entirety before using LipiView II. Failure to follow these instructions may result in improper use of the device.**

This manual provides essential information for safe and proper use of LipiView II.

- Section 2 (Important Device Information: indications, contraindications, warnings, precautions, potential adverse effects, device description, storage and transport, service and maintenance, cleaning, disposal and warranty)
- Section 3 (Instructions for Use for Start-up, First Time Setup, Lipid Imaging, Gland Imaging and Ocular Imaging)
- Section 4 (Troubleshooting Guide)

The ***LipiView II Administrator's Guide*** contains information about the setup and administration of LipiView II.

- **Prior to initial use of LipiView II, refer to Section 3.2 of this manual and/or the Administrator's Guide to ensure proper setup** (including requirements for operator (user) names, passwords, network connections and file storage.)

NOTE: LipiView II has a firewall and disabled remote access to protect the device and ensure privacy of patient records over a network. However, if LipiView II is connected to a non-secure wireless network, exported patient data will not be protected from unauthorized access. TearScience recommends the LipiView II be connected to a password-protected wireless router utilizing the WPA or WPA2 security protocols to ensure protection of the device and patient records.

Strong passwords do not contain words that appear in a dictionary, are at least six characters long, and consist of a mixture of letters and numbers. TearScience recommends that you choose a strong password and change it regularly (for example, every 90 days.)

Contact TearScience (in North America, at +1 919 459 4891 or by email at customerservice@tearscience.com) with any questions about the information contained in this manual or for additional information on the safe and proper operation of LipiView II.

2 Important Device Information

2.1 Indications for Use

The LipiView II Ocular Surface Interferometer is an ophthalmic imaging device intended for use by a physician in adult patients to capture, archive, manipulate and store digital images of:

- Specular (interferometric) observations of the tear film. Using these images, LipiView II measures the absolute thickness of the tear film lipid layer.
- Meibomian glands under near-infrared (NIR) illumination
- The ocular surface and eyelids under white illumination

2.2 Contraindications

Contraindications are conditions in which the device should not be used because the risk of use clearly outweighs any benefit. No contraindications have been identified for LipiView II.

2.3 Precautions

The following patient conditions may affect the interferometry assessment of a patient's tear film using LipiView II:

- **Use of ophthalmic drops such as artificial tear lubricants, ointments, and medications.** Advise patients not to instill oil-based ophthalmic drops (e.g., Soothe®, Restasis®, Systane Balance®) for at least 12 hours prior to device use and not to instill ointments for at least 24 hours prior to device use. Wait at least 4 hours after instillation of all other ophthalmic drops prior to device use.
- **Soft or rigid contact lens wear**. Advise patients to remove contact lenses at least 4 hours prior to device use.
- **Use of oil-based facial cosmetics around the eye.**
- **Eye rubbing.**
- **Recent swimming in a chlorinated pool.** Advise patients not to swim for at least 12 hours prior to device use.
- **Any ocular surface condition** that affects the stability of the tear film. These conditions include disease, dystrophy, trauma, scarring, surgery, or abnormality.

2.4 Warnings

Review the warnings in Table 1 prior to using LipiView II.

Table 1: General and Operation Warnings

GENERAL WARNINGS
WARNING: No modification of this equipment is allowed.
Caution: **Power Requirements.** The LipiView II is a continuous operation device which requires a power source of 100-240 Volts AC ± 10%, 50/60 Hz single phase, 4 Amps. Connection to a power supply other than a supply mains with protective earth may result in electric shock.
Caution: The LipiView II has protection against electric shock of applied part classified as Type B. This device is classified as an IEC Class 1 product.
Caution: **Voltage Protection and Fuse Selection.** Contact TearScience to replace a blown fuse. TearScience personnel must replace only with a 5 x 20 mm, 4 A, 300 ms, 40 A breaking capacity fuse to avoid risk of fire. TearScience personnel must disconnect from power before servicing to avoid risk of electrical shock.
Caution: Backup Battery Replacement**.** Backup battery cannot be replaced.
Caution: Keep the LipiView II away from strong magnetic fields as it could damage the device's hard drive, but is not a safety hazard to the user or patient.
Caution: This equipment is intended for use by healthcare professionals only. This equipment may cause radio interference or may disrupt the operation of nearby equipment. It may be necessary to take mitigation measures, such as re-orienting or relocating the LipiView II or shielding the location.
Caution: Portable and mobile RF communications equipment can affect MEDICAL ELECTRICAL EQUIPMENT.
Caution: The use of ACCESSORIES, transducers and cables other than those specified, with the exception of transducers and cables sold by the manufacturer of the EQUIPMENT or DEVICE as replacement parts for internal components, may result in increased EMISSIONS or decreased IMMUNITY of the EQUIPMENT or DEVICE.
Caution: The EQUIPMENT or DEVICE should not be used adjacent to or stacked with other equipment and if adjacent or stacked use is necessary, the EQUIPMENT or DEVICE should be observed to verify normal operation in the configuration in which it will be used.
Caution: Degree of protection against harmful ingress of liquid: IPX0. This equipment has no protection against ingress of liquids.
Caution: This device is not suitable for use in the presence of flammable mixtures.
Caution: This device is not suitable for use in oxygen rich environments.
Caution: The device monitor and base unit may exceed 41°C. Device will remain within safe momentary contact temperature, below 51°C.

 ***OPERATION WARNINGS***
Caution: Federal law restricts this device to sale by or on the order of a physician.
Caution: The chin and forehead rest surfaces and Handheld Near IR Lid Everter must be disinfected with alcohol immediately prior to use and prior to storage.
Caution: **Photo-toxicity hazard.** No acute optical radiation hazards have been identified for LipiView II under intended use conditions. Since prolonged intense light exposure can damage the retina, the use of the device for ocular examination should not be unnecessarily prolonged. The retinal exposure dose for a photochemical hazard is a product of the radiance and the exposure time. Aphakes and persons with diseased eyes will be at greater risk. The risk may also be increased if the person being examined has had any exposure with the same instrument or any other ophthalmic instrument using a visible or near-infrared light source during the previous 24 hours. ***Caution:*** The light emitted from this instrument is potentially hazardous. The longer the duration of exposure, the greater the risk of ocular damage. Exposure to light from the instrument when operated at maximum intensity will exceed the safety guideline after 8 hours.
Caution: To prevent pinching, do not put fingers near illuminator, lens or chin rest during focusing. Instruct patient not to place hands on LipiView II during operation, and not to put fingers near illuminator, lens or chin rest.
Caution: If a problem occurs with LipiView II, identify the symptom then attempt to resolve the problem as indicated in Section 4, *Troubleshooting Guide*. If the problem cannot be resolved, stop using the device and contact TearScience.
Caution: To prevent electric shock or performance alteration, do not attempt to service the device or remove the cover. No maintenance is required for LipiView II, and the device and all of its associated parts are not serviceable by the user.
Caution: In order to isolate this equipment from supply mains the equipment must be unplugged from the wall. Do not position the equipment in a location which would prevent the unit from being unplugged in an emergency.
Caution: Do not store this instrument in conditions where the temperature may rise above 55°C or fall below -10°C.
Caution: When lifting or handling LipiView II, caution should be taken to prevent injury or damage to the device. Prior to moving the device, put the monitor arm into a locked position and unplug the power cord from the wall. If an external monitor is attached, disconnect the external monitor prior to moving the device.
Caution: Shock hazard. Do not touch patient and device under top cover simultaneously**.**

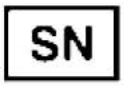
2.5 Potential Adverse Effects

There are no known or anticipated adverse effects associated with use of this device.

2.6 Labeling

Table 2 provides a description of the symbols used on LipiView II labeling.

Table 2. Symbols Used on LipiView II Labeling

Label Symbol	Symbol Description
	Type B applied part
	Consult operating instructions
	Device transmits radiofrequency (RF) energy
	Text consists of a warning or precaution relating to safety. Read the text carefully and use the equipment as instructed to ensure safety.
	Reference Number
	Serial Number
	**CAUTION**: Federal law restricts this device to sale by or on the order of a physician.
 0086	Mandatory conformity mark for medical device products in the European Economic Area (EEA). The **CE marking** certifies that a product has met consumer safety, health or environmental requirements. "0086" is the Notified Body Number.
	This model/product is Listed in Intertek's Directory of Listed Products.

Label Symbol	Symbol Description
	Date of Manufacture
	Manufacturer
	Temperature Limitation, defining upper and lower temperature limits; used for storage or shipping temperatures.
EC REP	Authorized Representative in the European Community
P/N	Part Number
Rev	Revision Level

2.7 Device Description and Overview

The LipiView II is a bench-top device used as an ophthalmic camera for imaging the lipid layer of the tear film, meibomian glands, ocular surface and eyelids. There are three imaging modes: Lipid, Gland and Ocular.

In Lipid Imaging Mode, LipiView II operates on the principle of white light interferometry and provides an interferometry color assessment of the tear film by specular reflection. The patient's eye is positioned in front of an illumination source directed toward the tear film on the corneal surface. Light from the illumination source passes through the tear film and is specularly reflected into a camera. The light reflecting back through the lens in the camera forms an interference pattern, called an "interferogram." A video image file is recorded over time since the interference pattern changes as the tear film is distributed across the cornea during blinking.

The computer system captures and enhances the interference pattern and displays a profile corresponding to an interferometry color scale. This color scale has been validated to a known standard for measurement of thin film thickness, demonstrating that LipiView II has the ability to make absolute thickness measurements of the tear film lipid layer by the imaging interferometric colors. The measured lipid layer thickness may range from 10 to 240 nanometers (nm), with a precision of 1 nm and an accuracy of ±10 nm. The conformance factor of the measured interference pattern is displayed as a "C-factor," which is equal to the proportion of measured colors that match the predicted interferometric color scale. The video image of the ocular surface may be viewed on the computer screen display and in a printed report.

In Gland Imaging Mode, LipiView II uses near infrared (NIR) illumination and an NIR-sensitive camera mounted on a motion control system to image the meibomian glands. The tissue between the meibomian glands and the surface of the eyelid are transparent to NIR light; the glands reflect NIR wavelengths, allowing them to be imaged.

In Ocular Imaging mode, LipiView II captures high-resolution still images or video to record relevant findings on the ocular surface and/or eyelids. The images can be taken using room light only or the device's built-in white light.

LipiView II contains the following components, which are identified in Figure 1 (Front/Patient View) and Figure 2 (Rear/User View):

- Base with Computer System and Electronics
- 2-position Forehead and Chin Rest with Fluted Roller (for height adjustment)
- Motion Stage
- Camera and Attached Lens
- Illuminator
- Pushbutton Controls
- Touchscreen Display with Pivoting Arm
- USB Ports
- Handheld Near Infrared (IR) Lid Everter, shown in Figure 3
- Connections for an External Monitor, the Near Infrared (IR) Lid Everter, and the power cord, shown in Figure 4.

Figure 1. Front (Patient) View of LipiView II

Key	
1	Forehead Rest

2	Camera and Attached Lens
3	Illuminator
4	Chin Rest
5	Fluted Roller (adjusts chinrest height)
6	Chin Rest Base -- 2-position (toward/away from device) adjust
7	Motion Stage
8	Back of Touchscreen Display
9	Pushbutton Controls (on top of unit)
10	Base (contains Computer System and Electronics)

Figure 2. Rear (User) View of LipiView II

Key	
1	Touchscreen Display
2	USB Port (another is on the other side, and a third is above the power switch)
3	Power Switch
4	Motion Stage
5	Chinrest --2-position (toward/away from device) adjust
6	Base (contains Computer System and Electronics)
7	Pivoting Arm

Figure 3. Handheld Near Infrared (IR) Lid Everter

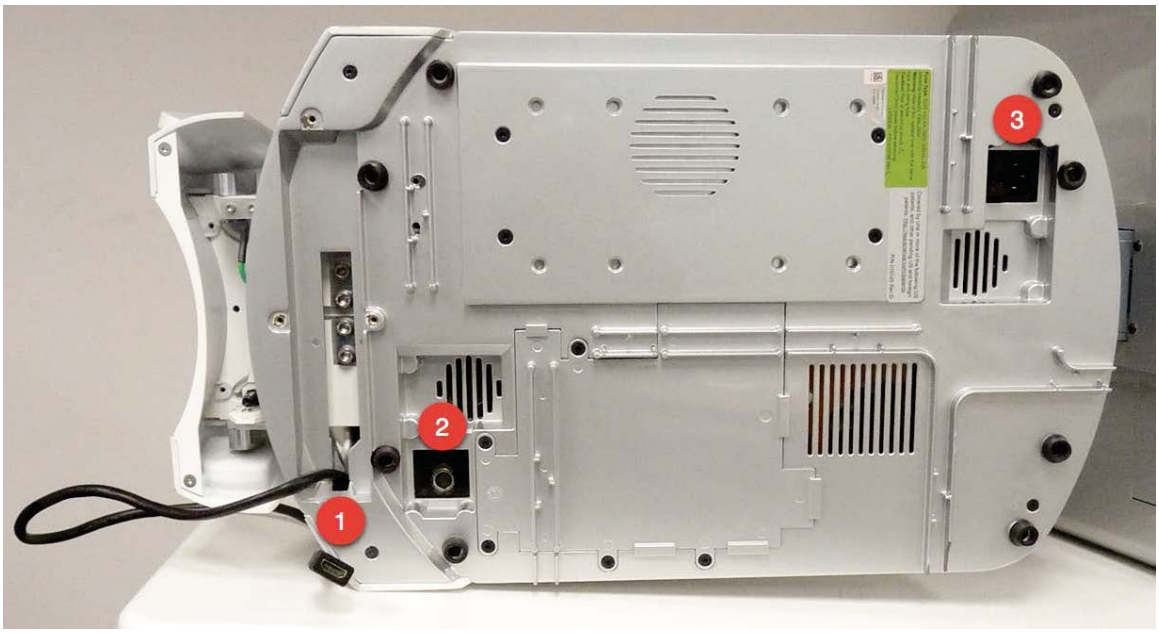


Figure 4. External Connectors on Underside of Base

Key	
1	Hardwired HDMI connection for external monitor
2	Connector for Handheld Near IR Lid Everter
3	Connector for Power Cord

2.7.1 Base with Computer System and Electronics

The base houses the power connection and computer hardware. The base connects with the forehead and chin rest, motion stage and touchscreen display. The on/off power switch (Figure

2) is located on the base opposite the chin rest. An external monitor connection is hardwired into the base, as is a connection point for the Near IR lid everter.

2.7.2 Forehead and Chin Rest with Fluted Roller

The adjustable forehead and chin rest is designed to allow proper positioning of the patient's head to capture images. To ensure a properly focused image, the patient must place his/her forehead and chin firmly against the forehead and chin rests. The chin rest may be raised or lowered to accommodate different facial dimensions by spinning the fluted roller. The chin rest has a 2-position adjust (toward the device for Lipid imaging and away from the device for Gland and Ocular Imaging.)

Two canthus alignment marks are located on the left and right sides of the forehead rest. Adjusting the chin rest to position the lateral canthus of the patient's eye at these marks will optimize the range of camera motion.

The forehead and chin rest come in contact with the patient. Disinfect the forehead and chin rest surfaces with alcohol immediately prior to use and prior to storage.

2.7.3 Motion Stage

The motion stage contains the camera, illuminator and motor controls used to adjust the camera and illuminator. The height of the motion stage is adjusted as part of the image capture process, to position the camera correctly.

2.7.4 Camera and Attached Lens

The camera is located inside the motion stage and is not visible externally. The height of the camera is adjusted as part of the motion stage. The camera can also be adjusted left and right and backwards and forwards with separate controls.

2.7.5 Illuminator

The grid-like fixture attached to the motion stage is the illuminator. The height of the illuminator is adjusted as part of the motion stage. There are no separate controls for the illuminator.

2.7.6 Pushbutton Controls

LipiView II includes a pushbutton control keypad on top of the unit that may be used in all modes, to make it easier for the operator to capture images.

2.7.7 Touchscreen Display with Pivoting Arm

The touchscreen display is on a pivoting arm, which allows it to be positioned ± 45 degrees or ± 90 degrees from its location shown in Figure 1. To reposition the screen, press the button under the pivoting arm while moving the arm left or right to the approximate 45 or 90 degree location. Release the button and continue moving the arm until it locks into place.

In addition to displaying images and information to the operator, the screen functions as a touchscreen user interface to the LipiView II. The operator touches the screen to operate the motion stage and camera controls and capture images.

2.7.8 USB Ports

The lower base of the touchscreen display contains three USB ports, located as shown in Figure 2. These ports may be used to connect a printer or storage device.

2.7.9 Handheld Near Infrared (IR) Lid Everter

The Handheld Near Infrared (IR) Lid Everter is both a near-infrared light source and a shaped instrument that aids in the proper eversion of the lower eyelid. The Near IR Lid Everter contacts the patient's lower eyelid. Inspect the Near IR Lid Everter to ensure it is intact prior to use. Disinfect the Near IR Lid Everter with alcohol immediately prior to use and prior to storage. Place the Near IR Lid Everter slightly below the lash line and move the instrument slightly inward and upward to evert the entire length of the lower eyelid.

2.7.10 Operating Environment and Specifications

System and environmental specifications are displayed in Table 3.

Table 3. System and Environmental Specifications

Input Voltage	100 – 240 VAC, 50 – 60 Hz
Product Safety Classification	Type B Applied Part
IEC 60601-1— Medical electrical equipment—Part 1: General requirements for safety	
IEC 60601-1-2 — Medical electrical equipment—Part 1: General requirements for safety—Section 2: Collateral standard—Electromagnetic compatibility—Requirements and tests;	CISPR 11 (Class A, Group 1)
Accuracy of lipid layer thickness measurement	±10 nm
Operating Temperature	10°C to 35°C
Operating Relative Humidity	Up to 90% non-condensing
Atmospheric Pressure	700 hPa to 1060 hPa
Storage Temperature	-10°C to 55°C
Transport Temperature	5°C to 60°C

2.7.11 Accessory Support

LipiView II may be used with the following USB accessories that are compatible with Windows 7 and USB 2.0:

- USB printer (Printer Support)
- USB external hard drive (External Backup Support)

- USB flash drive (USB / Thumb Drive Support)
- USB mouse and keyboard (support for optional alternative to touchscreen controls)

LipiView II is designed to operate wirelessly with other network devices, such as a printer. Placement of LipiView II should be within range of the network, if a network system is used.

LipiView II may be used with an external monitor. The hardwired connection in the base will support HDMI or DVI inputs for an off-the-shelf external monitor, which has at least 1280 x 1024 resolution and supports 60Hz frame rates.

2.8 Storage and Transport

Before storage, ensure the power switch is off, and the chin and forehead rest surfaces, as well as the Near IR Lid Everter, are cleaned according to the instructions in Section 2.10, *Cleaning*. Store LipiView II in a way that prevents contamination and damage between uses.

For transport, ensure power cord is unplugged and secured off the ground. Grip onto metal portion of the device in two locations: 1) under the base or under the head containing the motion stage; and 2) monitor arm behind the screen. Carefully lift and move the device in an upright position.

2.9 Installation, Maintenance and Servicing

There are no specific installation requirements for LipiView II, other than unpacking the device from its carton and connecting power and accessories (the external monitor and Near IR Lid Everter.) The device is installed and ready to use safely and correctly if it passes its Power-On Self Test with no system errors.

LipiView II performs a calibration process at startup. LipiView II does not require preventive maintenance or scheduled calibration. If the touchscreen gets out of calibration, refer to the *LipiView II Administrator's Guide* for instructions on how to recalibrate the touchscreen using the built-in utility.

Expected life of LipiView II is 5 years. Note that no user serviceable components are inside the unit. For Field Service, contact TearScience in North America at +1 919 459 4891 or by email at customerservice@tearscience.com.

2.10 Cleaning

Table 4 identifies the components of LipiView II that require cleaning. For each component, the frequency and method of cleaning is provided.

Table 4: LipiView II Cleaning Information

Component	Frequency	Method
Chin rest and forehead rest	Immediately prior to use and prior to storage	Alcohol

surfaces		
Handheld Near IR Lid Everter	Immediately prior to use and prior to storage	Alcohol
Camera lens and Illuminator	Monthly	Wipe with a lint-free photographic quality lens cloth
Touchscreen Display Monitor	When soiled or as needed	• Power off the device. • Apply window or glass cleaner to a cloth rag and wipe the screen • **Do not apply cleaner directly to the screen** • **Do not clean the monitor with alcohol, paint thinner, benzene or compressed air**
LipiView II exterior, including keypad	When soiled or as needed	• Wipe down exterior of the device with a mild soapy cloth • **Do not use bleach, chlorine or acetone-based solutions** to clean any part of the chin rest or the system enclosure
External monitor	Follow manufacturer's cleaning instructions	Follow manufacturer's cleaning instructions

2.11 Disposal

LipiView II consists of an ABS plastic enclosure, aluminum chassis, circuit boards, and electrical components. In the unlikely event that the device is damaged and cannot be repaired, never dispose of the device. Return LipiView II to TearScience using the contact information on the first page of this manual.

2.12 Warranty

TearScience, Inc. warrants that each LipiView II: 1) is free from defects in materials and workmanship; and 2) conforms to TearScience Inc.'s official specifications. The warranty period for each LipiView II is one year commencing on the date of purchase. *Any tampering or modifications to the device by the user will void the warranty.*

3 Instructions for Use

3.1 Startup and Login

At startup, LipiView II performs a self-test, confirms camera connection, verifies system voltages, checks remaining hard drive space, and calibrates camera motors.

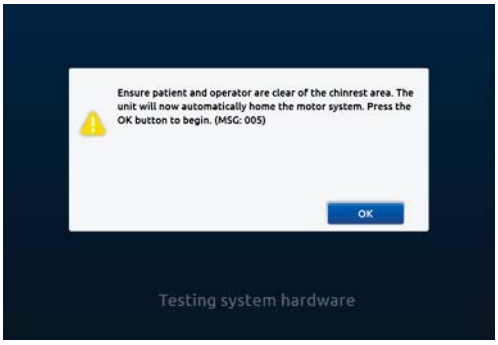


Figure 5. Warning Screen

Figure 6. Initialization Screen

Figure 7. Login Screen

1. Ensure the power cord is plugged into an electrical outlet. The power cord connection is located underneath the base of the device.

2. Power on LipiView II by pressing the rocker switch on the device base (refer to Figure 2). The touchscreen display is initially blank and then displays a "Welcome" message and other messages related to self-test and initialization.

3. Press the OK button to acknowledge the warning (Figure 5) after ensuring the patient and operator are clear of the chinrest area. The motion stage moves during system hardware self-test, which takes about 20 seconds.

4. Touch the screen to continue when Figure 6 is displayed indicating that the device is ready for use. (Note that the software version displayed may differ from Figure 6.)

5. When the Login screen (Figure 7) is displayed, enter the operator name and password using the onscreen keyboard. (Operator name and password are provided by the Administrator or TearScience trainer.) Press *Log In*.

3.2 First Time Device Setup

Prior to initial use, ensure that the following instructions are completed by an Administrator. Other administrative functions, detailed in ***LipiView II Administrator's Guide***, can be completed at the discretion of the Administrator. LipiView II has been set up with a default Operator Name (LIPIVIEW) and Password (LIPIVIEW) that has administrator privileges. After initial login, it is recommended but not required that the Administrator reset the password.

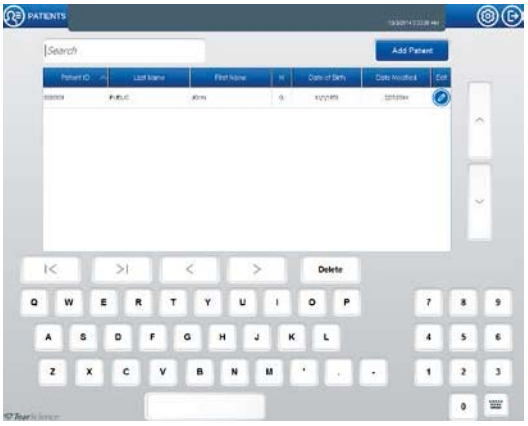


Figure 8. Patient Records Screen

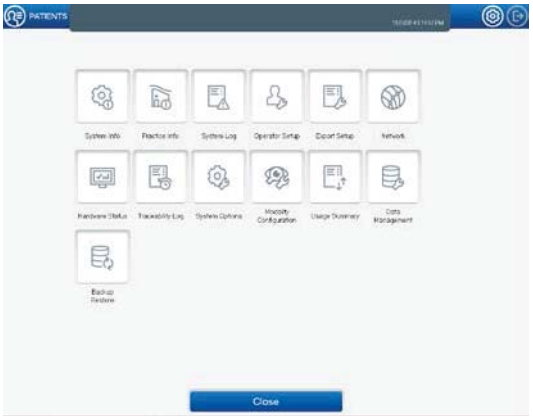


Figure 9. Main Admin Screen

1. Power on the system.
2. When the Login screen (Figure 7) is displayed, enter LIPIVIEW for both the Username and Password. (The onscreen keyboard only supports uppercase characters.) Press *Log In*. The Patient Records screen (Figure 8) is displayed.
3. Press the Gear icon [ ] on Menu bar (Figure 10) located in the upper right corner of the screen. The Main Admin screen (Figure 9) is displayed.
4. Press *Operator Setup*. Add additional operator usernames and set or change passwords as needed.

Before capturing images, it is also recommended that the following items be set up using the functions on the Main Admin screen (Table 5).

<u>From Main Admin screen (Figure 9):</u>

5. Press *Practice Info* to enter Practice Information.
6. Press *System Info*, then Press *Set Date and Time* to set System Date and Time.
7. Press *Network* to set up network connections.
8. Press *Close* to return to the Patient Records screen (Figure 8).

Table 5. Main Admin Functions

System Info	System information, including software versions and important utilities (Calibrate Touchscreen, Set Date and Time, Set Up System for Packaging, Launch Remote Support, Software Update, Save Changes and Shut Down, Save as PDF)
Practice Info	Enter the name and business information for the medical practice
System Log	View the system log, which collects information about key system events and errors (useful for troubleshooting and technical support)
Operator Setup	Add or delete Operators (users) and/or Administrator
Export Setup	Select file formats for records export
Network	View network information
Hardware Status	See comprehensive status information for the hardware and software
Traceability Log	View records of all traceable events to ensure data integrity (e.g., users added/deleted, treatment records moved from one patient to another)
System Options	Set the automatic logout timer, choose display options
Modality Configuration	Set options for Lipid Imaging or Gland Imaging modes
Usage Summary	View statistics about use, selected by configurable criteria
Data Management	Delete or move patient records (creates a permanent record in the Traceability Log)
Backup/Restore	Backs up or restores LipiView II patient and treatment data to networked drive or other media

3.3 Menu Bar

The menu bar (Figure 10), shown at the top of the screen, has the following icons.

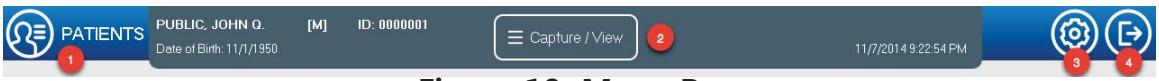


Figure 10. Menu Bar

Key	
1	***Patients Button*** – Touch to return to Patient Records screen (Figure 11)
2	***Drawer Dropdown*** – Contains information on current patient and active imaging session (if any). Pull down to access patient history. When on Image Capture screens or Review Image screens, press ***Capture/View Button*** on menu bar to return to Capture/View screen (Figure 13).
3	***Admin*** – Touch to access Administrator screens (requires access privileges)
4	***Log Out***

3.4 Enter and Select a Patient and Imaging Mode

After Login, enter a new patient or search for an existing patient. Select the patient to capture new images or view prior images. Then, select an imaging mode.

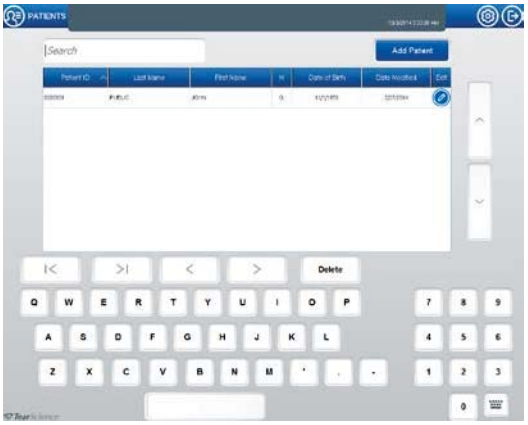


Figure 11. Patient Records Screen

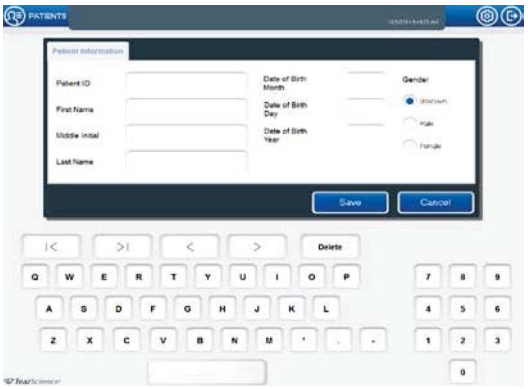


Figure 12. Patient Entry Screen

Figure 13. Capture/View Screen

1. For a ***New Patient***, select *Add Patient* on Patients Records screen (Figure 11) to display Patient Entry screen (Figure 12).

2. Using onscreen keyboard, enter patient information, then press *Save*. Patient records must include at a minimum:
   1) Patient ID or
   2) Last Name, First Name and Date of Birth (enter the month and date as two-digit numbers, and the year as a four-digit number: MM/DD/YYYY).

3. For an ***Existing Patient***, enter patient data (patient ID or name) in Search field on Patient Records screen (Figure 11) to locate the record. To edit patient data, press Pencil icon to the right of the list.

4. Select the desired patient record from the patient listing table.

   NOTE: The step keys can be used to move backwards or forwards through the table. When the list spans multiple pages, sort the table by pressing the header field by the desired column. Press the same header a second time to sort the table in the reverse order. A small triangle in the column header indicates the table is being displayed by this column. The triangle points down or up to specify the sorting direction.

5. When Capture/View screen (Figure 13) displays, select an imaging mode (Lipid Imaging, Gland Imaging or Ocular Imaging) to capture new images or view prior images for that patient. Select *All Exams* to view all images in the patient's history.

3.5 Capture Tear Film Images (Lipid Imaging Mode)

1. To image the tear film lipid layer by specular reflection of light, select Lipid Imaging from the Capture/View screen (Figure 13) and press *New*.
2. Disinfect the forehead and chin rest with alcohol prior to use.
3. Ensure the chin rest is in closest position toward the device.
4. Place the patient's chin fully forward into chin rest and forehead firmly against forehead rest. Adjust the height of the chin rest by spinning the fluted roller until the temporal canthus is aligned with the marks on the left and right sides of the forehead rest. Instruct the patient to look at the orange fixation light.

CAUTION: **To prevent pinching, do not put fingers near illuminator, lens or chin rest during focusing. Instruct patient not to place hands on LipiView II during operation, and not to put fingers near illuminator, lens or chin rest.**

5. Select OD (right eye) or OS (left eye) to image by touching the right or left side of the Lipid Image Capture screen (Figure 14).
6. Position the camera using one or a combination of methods: 1) If the pupil is visible on screen, press autoposition reticle to automatically center the camera on the pupil. 2) Touch the desired location (toward pupil) on screen, which will automatically move the camera and center on the location. 3) Press the manual position buttons, as needed, until the pupil appears in the center of the screen. (You may also use the keypad to position the camera.)

   NOTE: Ensure the lower lid margin is visible to evaluate partial blinking

7. Focus the camera using one or a combination of methods: 1) Press autofocus reticle to focus (*not necessary if reticle was already pressed to position camera*); 2) press fine focus buttons to adjust the focus until the tear film image is clear. (You may also use the keypad to focus the camera.)

   NOTE: If the tear film image is not in focus, invalid video data may be saved.

8. Press *Capture* button to begin recording approximately 20 seconds of video. The blinking red light indicates LipiView II is recording. Press *Capture* button again to stop recording prior to 20 seconds, if desired.
9. Instruct the patient to blink naturally or to perform a squeezed blink, as desired.
10. When recording is complete, the illuminator turns off. Press *Notes* to add any notes to images, if desired.
11. Review video using onscreen playback button. If image quality is suboptimal, delete video using Trashcan icon and recapture another image.
12. Repeat steps 5 to 11 to capture an image of the other eye, if desired.
13. Press *Analyze* to save and process the image(s).

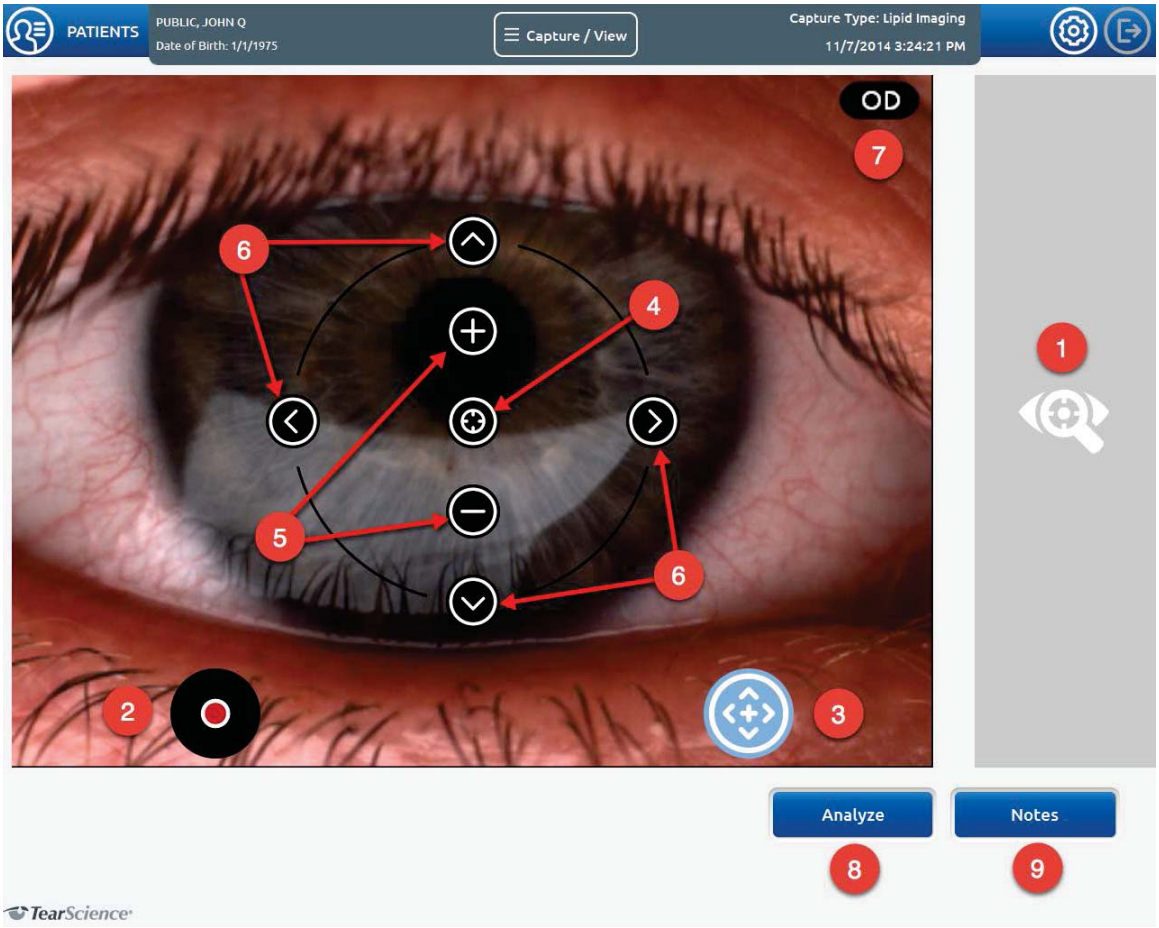


Figure 14. Lipid Image Capture Screen with Labeled Controls

Key	
1	***Magnify View Icon*** - OD (right eye) is currently in view. OS (left eye) side is currently greyed out. Touch icon to capture images for OS (left eye).
2	***Capture Video Button*** – Press to begin recording. Appears as a rectangle during recording; press rectangle to stop recording before 20 seconds.
3	***Select Position/Focus Button*** – Press to toggle display of manual focusing and positioning button controls on or off.
4	***Autoposition/Autofocus Reticle*** – Once the pupil is visible on screen, press the reticle to automatically center and focus the image.
5	***Manual Fine Focus Buttons*** - Press plus or minus to focus image
6	***Manual Positioning Buttons*** – Press to move camera left, right, up or down
7	***Eye Position Indicator*** – Indicates the eye being imaged (OD in figure)
8	***Analyze Button*** – Press to save, process and analyze captured imagery
9	***Notes Button*** – Press to open notes field for text entry

3.6 Review Tear Film Images (Lipid Imaging Mode)

1. After pressing *Analyze* on the Lipid Image Capture screen (Figure 14), the Review Lipid Images screen (Figure 17) appears with the tear film lipid layer images.
2. ***To review prior tear film lipid images for an existing patient***:
    a. Select the patient from the Patient Records screen (Figure 11).
    b. On the Capture/View screen (Figure 13), select Lipid Imaging to view prior lipid images or select All Exams to view all prior images.
    c. A list of prior images is displayed on the Capture/View screen (Figure 13). Drag and drop the desired images from the list to the sides of the screen marked "Drop Here". Touch the image again to display the Review Lipid Images screen (Figure 17).

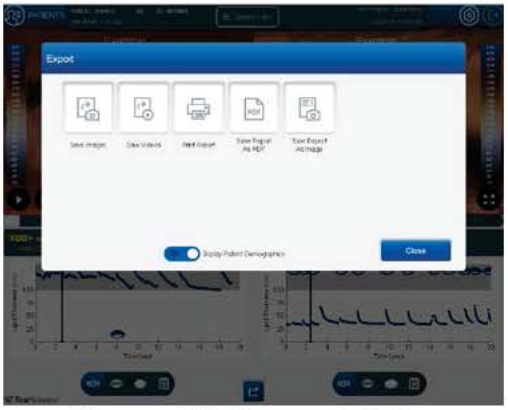


Figure 15. Export Dialog

3. Playback the video using onscreen controls.
4. If desired, press Export icon on the Review Lipid Images screen (Labeled 8 in Figure 17) to export or print images or report.
5. From the Export dialog (Figure 15), press the button to save images, video or report to an external medium or network, or print a report. Exported images can be displayed with or without patient demographics.

The Review Lipid Images screen (Figure 17) displays numerical and graphical analysis of the measured lipid layer thickness in nanometers (nm) from 10 (thinnest) to 240 (thickest), with a precision of 1 nm and an accuracy of 10 nm. The interferometric color scale (Figure 16) has been validated to a known standard for measurement of thin film thickness. By comparison to this known standard, the lipid layer thickness values are absolute thickness measurements of the tear film lipid layer.

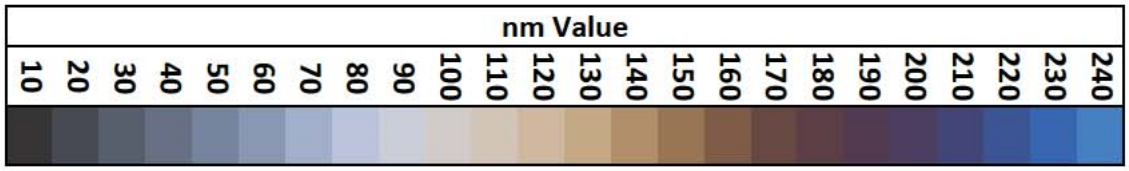


Figure 16. Interferometric Colors

NOTE: If analysis cannot be performed, a message *NO VALID ANALYSIS DATA FOR VIDEO* replaces the graph, and the numerical information shows as dashes (- - -).

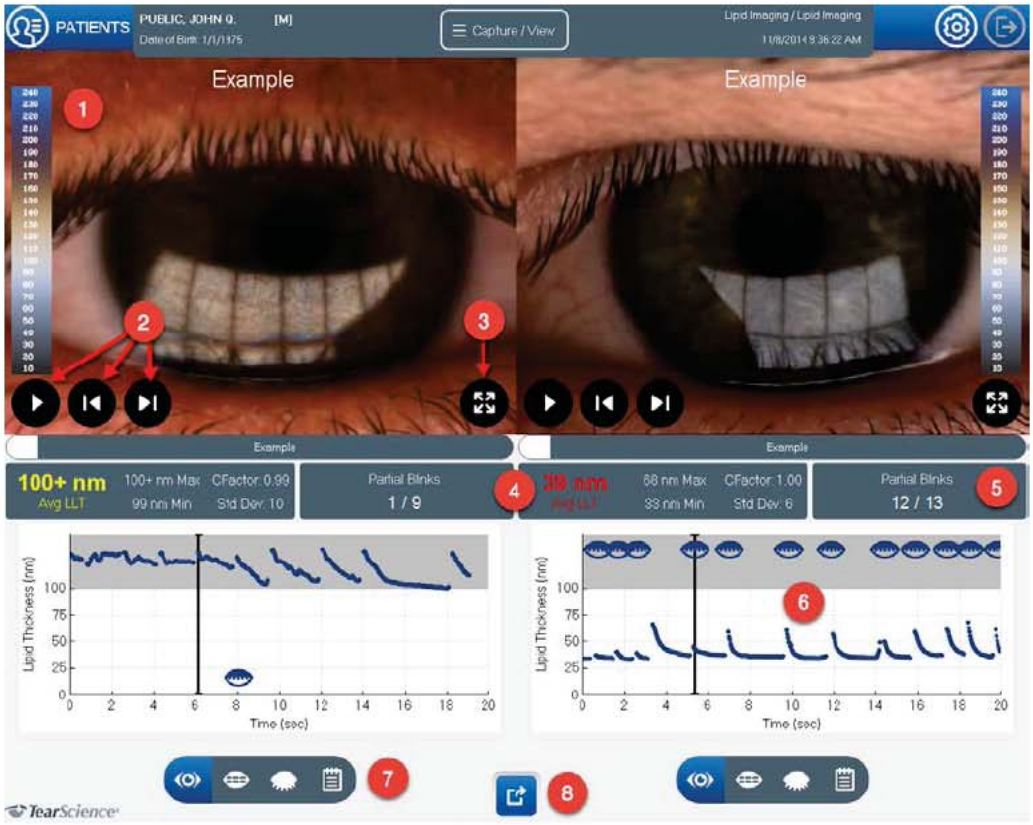


Figure 17. Review Lipid Images Screen with Labeled Controls

	Key
1	***Interferometric Color Scale*** - Corresponds to lipid layer thickness value in nm
2	***Video Playback Controls*** – Press to play, pause, forward step, reverse step
3	***Full Screen Mode*** – Press to view screen in full screen mode
4	***Numerical Analysis:*** • **Avg LLT:** Average lipid layer thickness in nm displayed in colored font corresponding to thickest (yellow), medium thickness (orange) and thinnest (red).[1] • **Max:** Maximum lipid layer thickness in nm recorded for a given video frame. • **Min:** Minimum lipid layer thickness in nm recorded for a given video frame. • **C-Factor:** Conformance factor is the ratio of image pixels that fall on the interferometric color spectrum. C-factor of 1.0 indicates every tear film pixel throughout the entire video has found a close match to an interferometric color. • **St Dev:** Standard deviation of the frame averages for lipid layer thickness. **NOTE:** Since most tear film images have an average thickness well below 100, the maximum thickness values displayed are 100 with values above 100 represented as "100+".
5	***Partial Blinks Count*** - Presented as a fraction with the number of partial blinks (numerator) over the number of total blinks (denominator). In this OD example, 1 partial blink/9 total blinks.
6	***Graphical Analysis:*** • Blue line shows average lipid layer thickness values over video sampling time. • Partial Blink Eye icon represents video frame where partial blink occurred.
7	***Select View Mode***: Press to toggle between Full Eye View (Eyeball icon), Isolated Tear Film View (Tiled icon), Blinking Frames Only View (Closed Eye icon) or Notes (Notepad icon).
8	***Export Icon*** – Export saved images, video or report to external medium or print report

[1] Finis D, Pischel N, Schrader S, Geerling G. Evaluation of lipid layer thickness measurement of the tear film as a diagnostic tool for Meibomian gland dysfunction. Cornea. 2013; 32(12):1549-53.

The first images, labeled as "Example" on the Capture/View screen (Figure 13), are standard reference video images of eyes with different lipid layer thickness values, provided for purposes of comparison. These videos allow the physician to observe differences in interference colors for a variety of tear films. As shown in Figure 18, the thin lipid example image is an example of an average tear film lipid layer thickness of 39 nm, which is relatively thinner lipid layer with very little color appearing mostly gray. Conversely, the thick lipid example image (Figure 19) is an example of an average tear film lipid layer thickness above 100, where brown and blue colors are visible indicating a relatively thicker lipid layer.

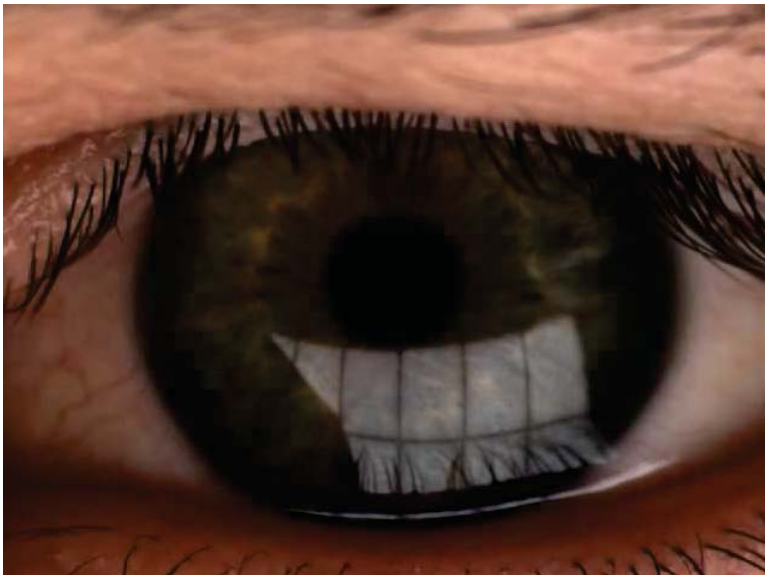


Figure 18. Example OD Image – Average Lipid Layer Thickness 39 nm

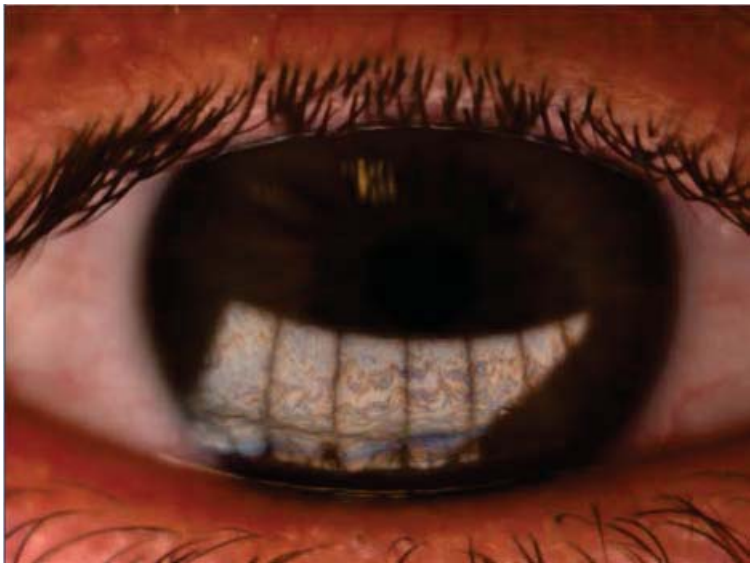


Figure 19. Example OS Image – Average Lipid Layer Thickness 100+ nm

3.7 Capture Gland Images (Gland Imaging Mode)

NOTE: One person can both evert the lids and operate the device, using the pushbutton controls on the top panel with an external monitor positioned behind the patient where the operator can easily see it. Alternatively, imaging the meibomian glands can be easier to perform as a two-person procedure: one person everting the eyelids, and one person operating and focusing LipiView II.

1. To image the meibomian glands, select Gland Imaging from the Capture/View screen (Figure 13) and press *New*.
2. **Turn the room lights off** (or down sharply) prior to imaging to ensure good contrast in the image quality.
3. Disinfect the forehead and chin rest and Handheld Near IR Lid Everter with alcohol prior to use. Inspect Handheld Near IR Lid Everter to ensure it is intact prior to use.
4. Ensure the chin rest is in the extended position away from the device (closer to the patient).
5. Place the patient's chin fully forward into chin rest and forehead firmly against forehead rest. Adjust the height of the chin rest by spinning the fluted roller until the temporal canthus is aligned with the marks on the left and right sides of the forehead rest.
6. Select the upper or lower eyelid of the OD (right eye) or OS (left eye) to image by touching the magnify view icon in the applicable quadrant on Gland Image Capture screen (Figure 22). (You may also use the buttons on the keypad.)
7. Carefully evert the eyelid and ensure that the full extent of the meibomian glands is visible over the entire nasal to temporal length of the eyelid.

    a. Evert entire length of lower eyelid: place Handheld Near IR Lid Everter (Figure 20) slightly below lash line; while maintaining contact, pull the lid down and then roll instrument slightly inward and upward.

    b. Evert upper lid at the top of the tarsal plate: use a cotton swab, finger or other handheld instrument (Figure 21). Ensure the fingertip or cotton swab is not blocking the inner surface of the eyelid before capturing the image.

Figure 20. Everting Lower Eyelid using Handheld Near IR Lid Everter

Figure 21. Everting Upper Eyelid using Cotton Swab

8. Position the camera using onscreen or pushbutton controls (Figure 23) on top of the unit to center the image of the everted eyelid on the screen. Alternatively, when using the touchscreen, touch the desired location to center the image on the screen and the device will automatically center the image in that location.

9. Press the autofocus reticle to focus the image using onscreen or pushbutton controls. If needed, press fine focus onscreen controls until the image is clear. (The F3 and F4 buttons on the keypad can also be used for fine focus.)

NOTE: Ensure full extent of the glands is visible over entire nasal to temporal length of the eyelid. When imaging lower eyelid, toggle between **Reflected IR** and **Trans IR** views (Figure 24) to ensure both views are of good image quality.

10. Press *Capture* button using onscreen or pushbutton controls to capture image.

11. Review gland image to ensure good image quality, including in both Reflected IR and Trans IR views for lower lid images (as shown in Figure 24). If the image is suboptimal (e.g., blurred focus, poor centration, only a partial lid eversion, finger obscuring view, washed out), delete image by selecting the Trashcan icon and recapture the image. Press *Notes* to add any notes to images, if desired.

12. Repeat steps 6 to 11 to capture the remaining images of other eyelid locations until all four eyelid images (i.e., upper and lower eyelid of the right and left eyes) are captured for the patient, if desired.

13. Press *Analyze* to save the image(s).

NOTE: PRESSING ANALYZE IS REQUIRED TO SAVE ALL IMAGES.
If *Analyze* is not pressed before exiting the imaging screen, a message will appear as a reminder to save the images.

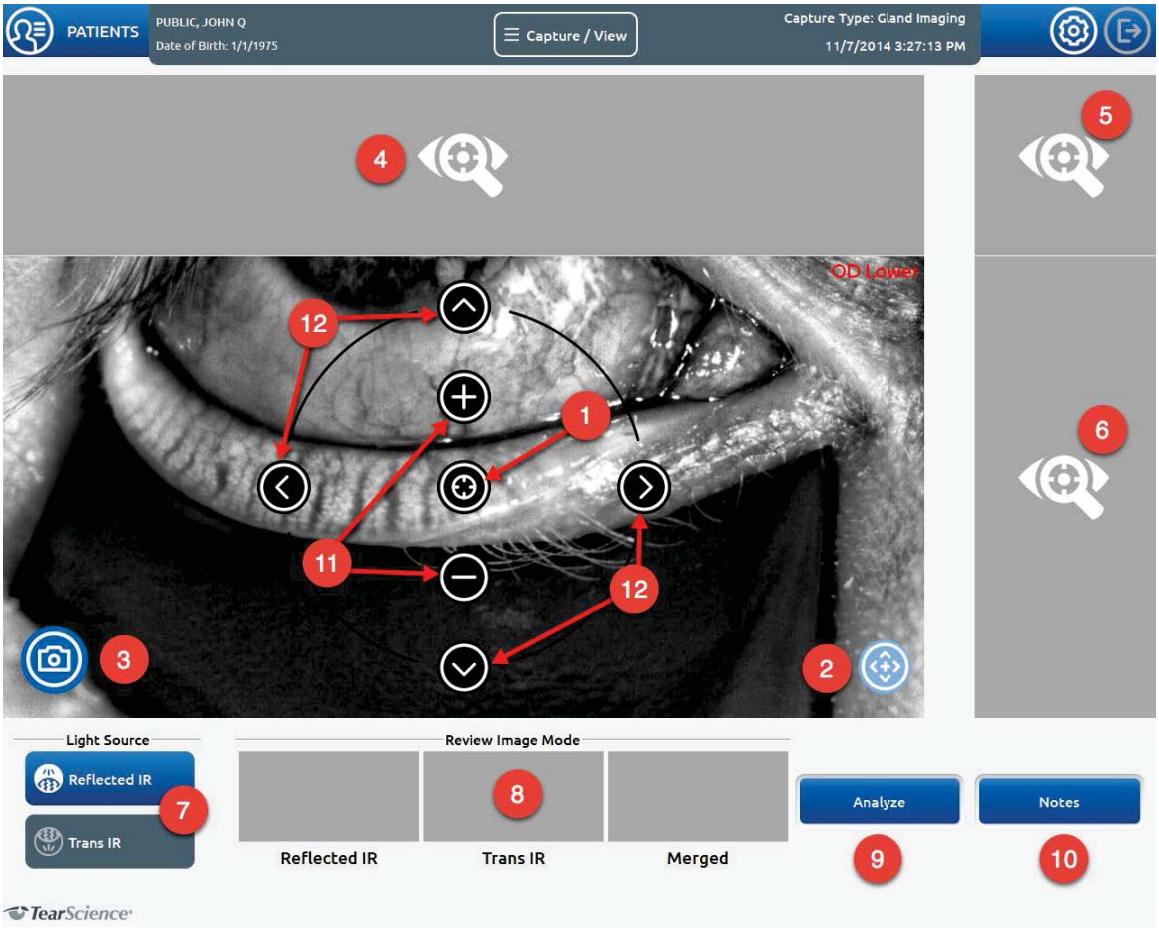


Figure 22. Gland Image Capture Screen with Labeled Controls

Key	
1	***Autofocus Reticle*** - Press the reticle to automatically focus the image
2	***Select Position/Focus Button*** – Press to toggle display of manual focusing and positioning button controls on or off
3	***Camera Button*** – Press to capture still image
4	***Magnify View Icon*** - OD (right eye) lower lid is currently in view Touch to image OD (right eye) upper lid.
5	***Magnify View Icon*** - Touch to image OS (left eye) upper lid
6	***Magnify View Icon*** - Touch to image OS (left eye) lower lid
7	***Light Source*** - Toggle between Reflected IR and Trans IR illumination views to image lower lid. Only Reflected IR illumination is used for upper lid.
8	***Review Image Mode*** - Preview Captured Reflected IR, Trans IR and Merged images (after image capture, these small windows are populated with thumbnails of the different images)
9	***Analyze Button*** – Press to save captured imagery
10	***Notes Button*** – Press to open notes field for text entry
11	***Manual Fine Focus Buttons*** - Press plus or minus to focus image
12	***Manual Positioning Buttons*** – Press to move camera left, right, up or down

Gland Image Modes:

- **Reflected IR view** is shown for both upper and lower eyelid gland images.
- **Trans (Transillumination) IR view** is shown only for lower eyelid gland images, if images were captured using Handheld Near IR Lid Everter.
- **Merged view** is the combination of the Reflected IR and Trans IR views and is shown only for the lower eyelid gland images.

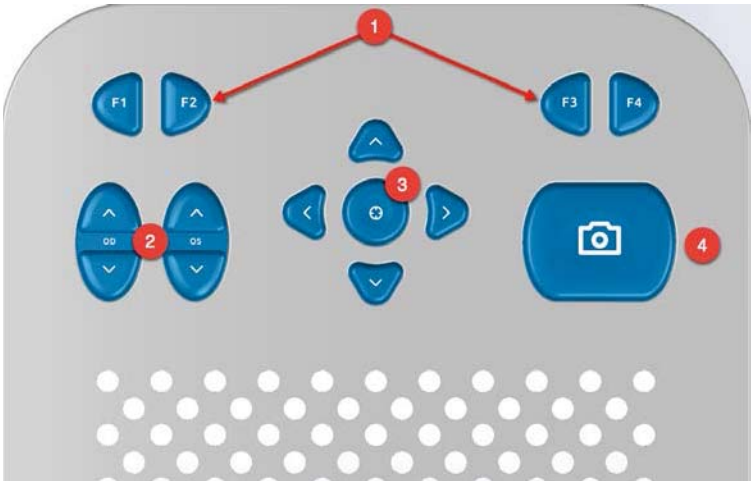
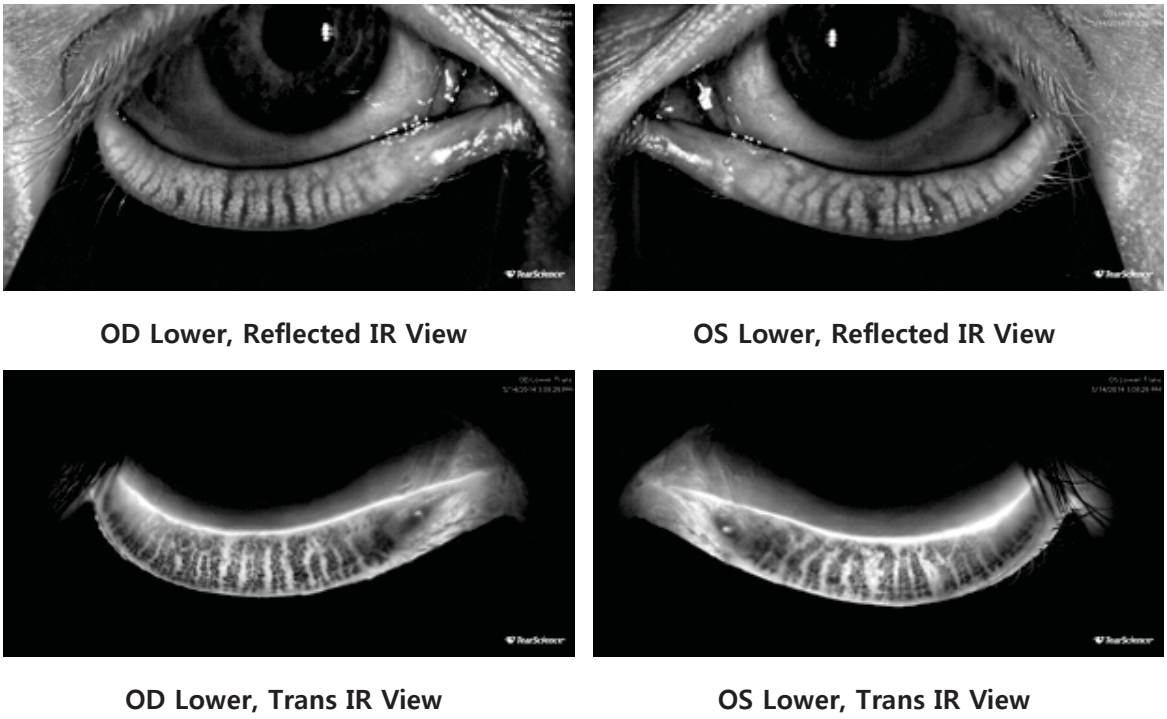


Figure 23. Pushbutton Controls (on top of unit)

Key	
1	**Function Keys** **F1:** In pre-capture view, toggles between Reflected IR and Trans IR mode **F2:** In post-capture review, changes view mode to captured Reflected IR image **F3:** In pre-capture mode, focuses in; post-capture review, changes view mode to captured Trans IR image **F4:** In pre-capture mode, focuses out; In post-capture review, changes view mode to captured Merged image
2	***Select Eye/Lid*** - OD for right eye or OS for left eye and upper or lower lid
3	***Position/Autofocus Buttons*** – Press up, down, right and left buttons to center on the desired lid. Tap to move in small increments or hold button down to move until released. Once lid is positioned, press reticle to autofocus.
4	***Camera Button*** – Press to capture an image



OD Lower, Reflected IR View | OS Lower, Reflected IR View

OD Lower, Trans IR View | OS Lower, Trans IR View

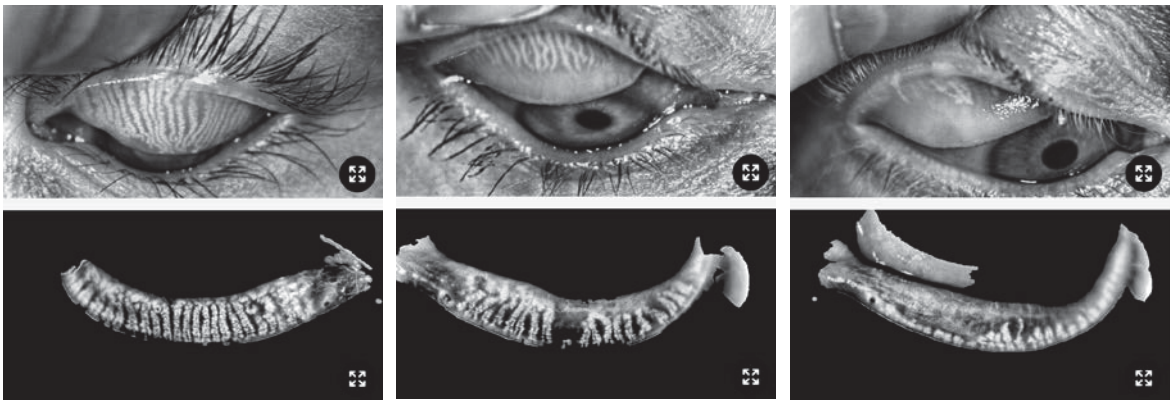
Figure 24. Properly Focused Lower Lid Images: Reflected IR and Trans IR

3.8 Review Gland Images (Gland Imaging Mode)

1. ***To review prior gland images for an existing patient***:
   a. Select the patient from the Patient Records screen (Figure 11).
   b. On the Capture/View screen (Figure 13), select Gland Imaging to view prior gland images or select All Exams to view all prior images.
   c. A list of prior images is shown on the Capture/View screen (Figure 13). Drag and drop the desired images from the list to the sides of the screen marked "Drop Here". Touch the image again to display the Review Gland Images screen (Figure 27).
2. If desired, press the Export icon at the bottom of the Review Gland Images screen (Labeled 4 in Figure 27) to export or print images or report.
3. From the Export dialog (Figure 15), press the button to save images or report to an external medium or network, or print a report. Exported images can be displayed with or without patient demographics.

The first images, labeled as "Example" on the Capture/View screen (Figure 13), are standard reference images of upper and lower eyelids with different gland findings, provided for purposes of comparison. As shown in Figure 25, the image set labeled high dropout is an example of an eye with severely truncated meibomian glands. The image set labeled as medium dropout is an example of an eye with some evidence of gland loss. The image set labeled as no dropout is an

example of an eye with no signs of gland loss. In Figure 26, the lower lid image labeled as dilation is an example of glands that appear dilated (enlarged), indicating a possible structural change or blockage.



No Dropout | Medium Dropout | High Dropout

Figure 25. Gland Example Images: No Dropout, Medium Dropout, High Dropout

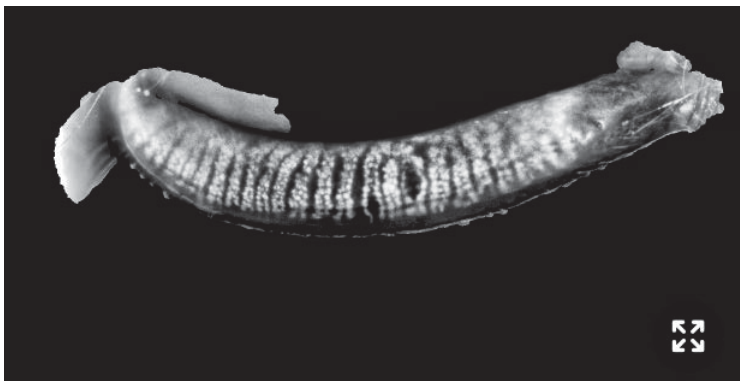


Figure 26. Gland Dilation Example, Lower Lid

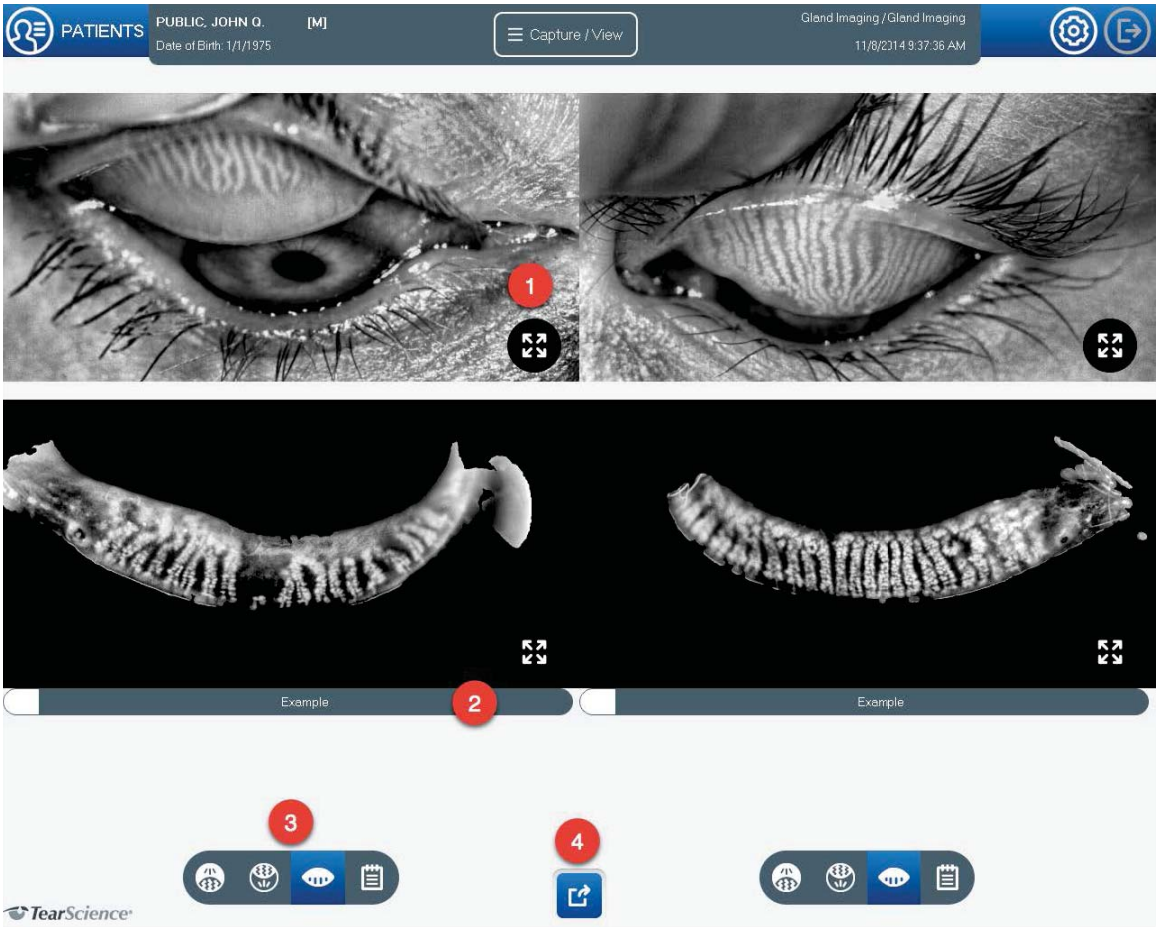


Figure 27. Review Gland Images Screen with Labeled Controls

Key	
1	***Full Screen Mode*** – Press to view screen in full screen mode
2	***Image Details*** – Timestamp date of image collection and Operator name
3	***Select View Mode***: Press to toggle between views; • **Reflected IR view** (Light from above icon) • **Trans IR view** (Light from below icon) – only displayed for lower lid images captured using Handheld Near IR Lid Everter • **Merged view** (Lower Eyelid icon) – only displayed for lower lid images captured using Handheld Near IR Lid Everter • **Notes** (Notepad icon)
4	***Export Icon*** – Export saved images or report to external medium or print report

3.9 Capture Ocular Images (Ocular Imaging Mode)

In Ocular Imaging mode, high-resolution images of the surface of the eye or the eyelids can be taken. White-light illumination may be switched on or off.

1. To image the ocular surface or eyelids, select Ocular Imaging from the Capture/View screen (Figure 13) and press *New*.
2. Disinfect the forehead and chin rest with alcohol prior to use.
3. Ensure the chin rest is in the extended position away from the device.
4. Place the patient's chin fully forward into chin rest and forehead firmly against forehead rest. Adjust the height of the chin rest by spinning the fluted roller until the temporal canthus is aligned with the marks on the left and right sides of the forehead rest. Instruct the patient to look at the orange fixation light.

CAUTION: **To prevent pinching, do not put fingers near illuminator, lens or chin rest during focusing. Instruct patient not to place hands on LipiView II during operation, and not to put fingers near illuminator, lens or chin rest.**

5. Select OD (right eye) or OS (left eye) to image by touching the right or left side of the Ocular Image Capture screen (Figure 28).
6. Select to turn white light illumination on, or turn off to capture images using room illumination only.
7. Position the camera by touching the desired location to be imaged on screen, which will automatically move the camera and center on the location. Press the position keys, as needed, until the location appears in the center of the screen.
8. Press the reticle to autofocus, or press the fine focus buttons to adjust the focus until the image is clear.
9. Press *Camera* icon to capture a still image. Press *Capture Video* button to begin recording approximately 5 seconds of video. The blinking red light indicates LipiView II is recording video. Press C*apture Video* button again to stop recording prior to 5 seconds, if desired. You can capture up to 10 still images and one video per eye.
10. When recording is complete, the illuminator turns off (if white illumination was turned on during imaging). Press *Notes* to add any notes to images, if desired.
11. Review still image or video using onscreen playback button. If image quality is suboptimal, delete image using Trashcan icon and recapture another image.
12. Repeat steps 5 to 11 to capture an image of the other eye, if desired.
13. Press *Save* to save the video or image(s).

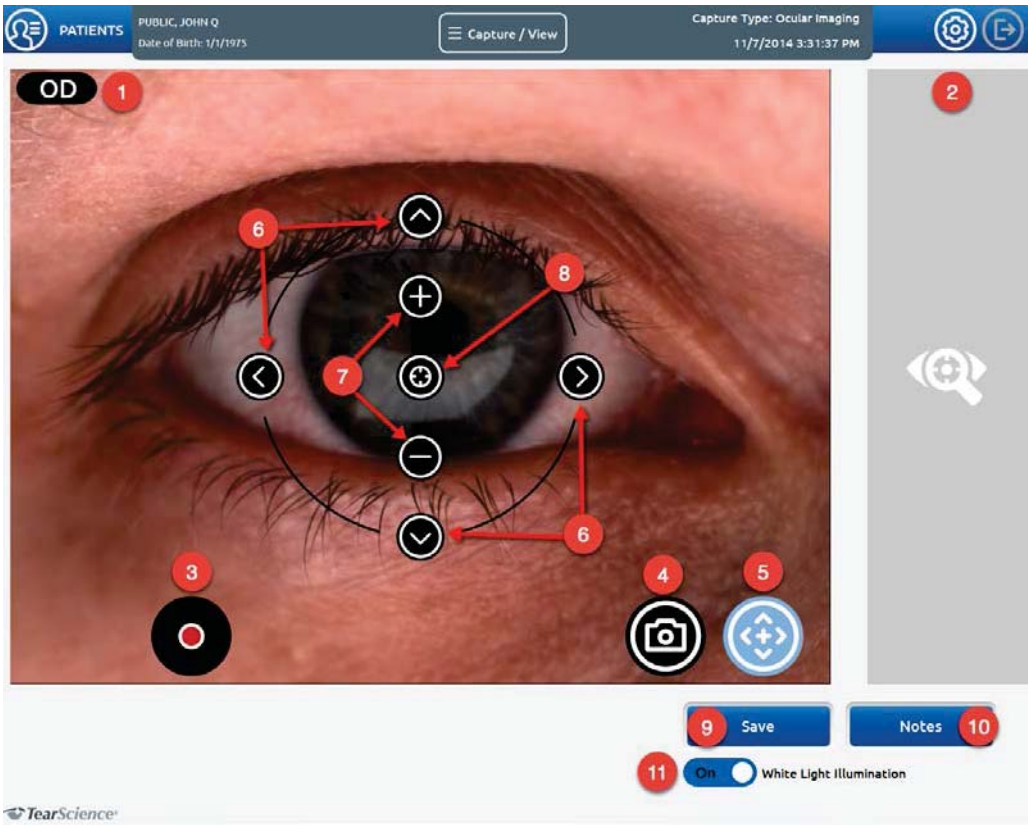


Figure 28. Ocular Image Capture Screen with Labeled Controls

	Key
1	***Eye Position Indicator*** **–** Indicates the eye being imaged (OD in figure)
2	***Magnify View Icon*** **–** OD (right eye) is currently in view. OS (left eye) side is currently greyed out. Touch icon to capture images for OS (left eye).
3	***Capture Video Button*** **–** Press to begin recording. Appears as a rectangle during recording; press rectangle to stop recording before 10 seconds.
4	***Camera Button*** – Press to capture still image
5	***Full Screen Mode*** – Press to view screen in full screen mode
6	***Manual Positioning Buttons*** – Press to move camera left, right, up or down
7	***Manual Fine Focus Buttons*** - Press plus or minus to focus image
8	***Autofocus Reticle*** **-** Press the reticle to automatically focus the image
9	***Save Button*** – Press to save captured imagery
10	***Notes Button*** – Press to open notes field for text entry
11	***White Light Illumination*** – Press to toggle illuminator on or off

3.10 Review Ocular Images (Ocular Imaging Mode)

1. ***To review prior ocular images or video for an existing patient***:
   a. Select the patient from the Patient Records screen (Figure 11).
   b. On the Capture/View screen (Figure 13), select Ocular Imaging to view prior ocular images or select All Exams to view all prior images.
   c. A list of prior images is shown on the Capture/View screen (Figure 13). Drag and drop the desired images from the list to the sides of the screen marked "Drop Here". Touch the image again to display the Review Ocular Images screen (Figure 29).
2. If desired, press the Export icon on the Review Ocular Images screen (Labeled 6 in Figure 29) to export or print images or report.
3. From the Export dialog save, (Figure 15), press the icon to save images, video or report to an external medium or network, or print a report. Exported images can be displayed with or without patient demographics.

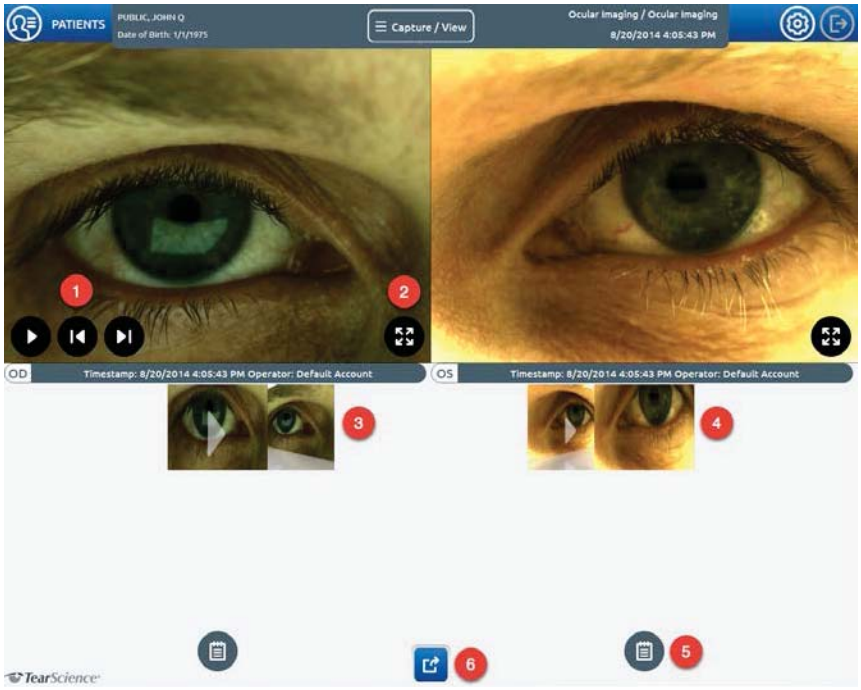


Figure 29. Review Ocular Images with Labeled Controls

Key	
1	***Video Playback Controls*** – Press to play, pause, forward step, reverse step (for captured video only)
2	***Full Screen Mode*** – Press to view screen in full screen mode
3	***Video Preview***
4	***Image Preview***
5	***Notes Button*** – Press to open and view notes field for text entry
6	***Export Icon*** – Export saved images, video or report to external medium or print report

3.11 Log Out and Power Off

Press the Log Out tab (Labeled 4 in Figure 10) on the menu bar to log out when the device is not is use.

Power off LipiView II overnight to allow the device to cool down. The device does not need to be powered off between patient examinations during the day.

4 Troubleshooting Guide

Table 6 lists the troubleshooting actions for Unexpected Events. For technical support, contact TearScience in North America at +1 919 459 4891 or by email at customerservice@tearscience.com.

Table 6: Troubleshooting Unexpected Events

Event	Action to Take
Device will not power up (after pressing the power switch, the screen remains dark)	Ensure device is connected to a power outlet and the connection into the device is secure, then press the power switch again. If the problem persists, contact TearScience.
Problem reported during Power On Self Test (POST)	Turn the device off then on again. If the problem persists, contact TearScience.
Touch Screen does not respond	Turn the device off then on again. If the problem persists, contact TearScience.
Illuminator does not light during lipid image capture	Turn the device off then on again. If the problem persists, contact TearScience.
Camera stops working	Turn the device off then on again. If the problem persists contact TearScience
Disk Space Indicator shows internal disk drive is full	Contact the Administrator to archive data. If the problem persists, contact TearScience.
The system works except the Capture screen will not respond (for Lipid, Gland, or Ocular Imaging)	An error was detected during power on self-test, which affects image acquisition. Turn the device off then on again. If the error persists, contact TearScience.
Device will not process images after acquisition	The internal hard drive is full. Contact the site Administrator to archive data. If the problem persists, contact TearScience.
Device no longer allows image acquisition	A power on self-test problem has been found. If the problem persists, contact TearScience.
The Review Lipid Images screen does not display a numerical lipid layer thickness value	The patient's head may not have been pushed forward, the patient's forehead may not have been firmly pressed against the forehead rest, or the tear film image may have been out of focus. Collect another video of the patient after ensuring that the patient's head is positioned properly and that the image is clearly focused.
Network is not connected	Contact the Administrator. If the problem persists, call TearScience.

Event	Action to Take
External monitor does not work	Ensure the monitor is powered on before LipiView II. Ensure connections to the DVI or HDMI are made, and proper video input is selected. Ensure the Administrator has activated and properly configured the monitor on the Computer Info screen in the Admin interface.
Administrator forgets password after resetting it	Contact TearScience.
When accessing options on the System Information Administration screen, this message displays: "Too much time has elapsed since system startup to access this function"	Selected options on the System Information Administration screen cannot be accessed after more than 10 minutes has elapsed since the system was started. Turn the device off then on again. Then, attempt to access the option again on the System Information Administration screen.
When accessing the Capture/View screen, a message displays stating disk space usage has surpassed the warning level	The system's disk drive usage is beyond the level specified in the Networking/Backup Administration screen. Contact the Administrator to perform a system backup.
When accessing the Capture/View screen, a message displays stating disk space usage has surpassed the critical level	The system's disk drive usage is beyond the maximum level specified by TearScience. Contact the Administrator to perform a system backup. Video capture is disabled until system backup is performed.

Table 7 describes the Operational System Messages categorized by type as: "E" for Error Message; "C" for User Confirmation Message; and "I" for Information Message Requiring User Attention. For a list of system messages related to System Administrative functions, refer to ***LipiView II Administrator's Guide***.

System messages are generated when something unexpected occurs, when the user attempts to perform an invalid operation, or to confirm completion of an event. These messages may instruct the user on a particular action to take (e.g., enter a missing field, or correct the format of a date field). When a system message is displayed, it requires a response from the user by pressing a button (e.g., Close or OK) on the message before any other input from the screen is accepted. System messages related to Windows error codes will also be listed in the System Log.

Table 7. Operational System Messages and Descriptions

ID	Type	Displayed Text	Description
1	E	You must enter a user name and password.	Displayed on Login screen if operator touches Login button without entering a username or a password
2	E	Invalid user name or password.	Displayed on Login screen if operator enters and invalid username and/or password and attempts to login to the system.
3	E	An internal system error was	Displayed on Login screen if the system database is corrupt

ID	Type	Displayed Text	Description
		encountered when attempting to log operator into system. Consult the system log for details.	and the system is unable to log an operator into the system. Service call or remote support is required to fix.
4	E	An internal system error was encountered when attempting to access the patient list. Consult the system log for details.	Displayed on Patient Records screen if the system database is corrupt and the system is unable to obtain a list of patients. Service call or remote support is required to fix.
5	I	Ensure patient and operator are clear of the chinrest area. The unit will now automatically home the motor system. Press the OK button to begin.	Displayed on Warning Screen during the system power-on self-test before the system performs initialization.
6	E	An error was encountered obtaining the list of network adapters. Consult the system log for details.	Displayed on Networking Administrator screen if the system is unable to obtain a list of network adapters from the operating system. Service call or remote support is required to fix.
7	E	An error was encountered obtaining the status of a network adapter. Consult the system log for details.	Displayed on Networking Administrator screen if the system is unable to obtain the status of the network adapters from the operating system. Service call or remote support is required to fix.
8	E	Image capture functionality has been disabled due to a system error. Consult the system log for details.	Displayed on Capture Screen if a system error has prevented new images from being captured. Reboot the system to see if the error clears. If the error does not clear, service call or report support is required.
9	E	The Capture screen is not configured correctly. Contact TearScience for technical support.	Displayed on Capture screen if the system database is corrupt and the Capture screen cannot reads its configuration. Service call or remote support is required to fix.
10	E	Unable to set up the system for image capture. Consult the system log for details.	Displayed on Capture screen if an error was encountered from the system hardware while attempting to configure the system to capture images. Try to enter the Capture screen again to see if the error clears. If the error does not clear, a service call or remote support is required to fix.
11	E	The live video stream from the camera has been interrupted. Please exit the Capture screen and try again. Consult the system log for details.	Displayed on Capture screen if an error was encountered from the camera during live video streaming. Try to enter the Capture screen again to see if the error clears. If the error does not clear, a service call or remote support is required to fix.
12	E	A motion control error was encountered. Consult the system log for details.	Displayed on Capture screen if an error was encountered trying to move a motion control axis. Try to enter the Capture screen again to see if the error clears. If the error does not clear, a service call or remote support is required to fix.
13	E	An error was encountered during video capture. Consult the system log for details.	Displayed on Capture screen if an error was encountered during video capture. Try to enter the Capture screen again to see if the error clears. If the error does not clear, a service call or remote support is required to fix.
14	E	The patient's date of birth is invalid. Please enter a valid date of birth.	Displayed on Patient Records screen if a patient is added or edited and an invalid date of birth in entered for the patient.
15	E	A first name must be entered for the patient.	Displayed on Patient Records screen if a patient is added or edited and the first name is omitted without a patient ID having been entered.
16	E	A last name must be entered for the patient.	Displayed on Patient Records screen if a patient is added or edited and the last name is omitted without a patient ID having been entered.

ID	Type	Displayed Text	Description
17	E	A first and last name plus a date of birth, OR a Patient ID, must be entered for the patient.	Displayed on Patient Records screen if a patient is added or edited and the patient ID is omitted.
18	E	The entered Patient ID already exists for another patient.	Displayed on Patient Records screen if a patient ID is entered for a patient and the patient ID is already used by another patient in the system.
19	E	An internal system error was encountered when attempting to add the patient to the system. Consult the system log for details.	Displayed on Patient Records screen if a system database error prevented system from adding a new patient. Service call or remote support is required to fix.
20	E	An internal system error was encountered when attempting to update the patient demographics. Consult the system log for details.	Displayed on Patient Records screen if a system database error prevented the system from editing an existing patient. Service call or remote support is required to fix.
21	E	An internal system error was encountered when attempting to perform the analysis. Consult the system log for details.	Displayed on Capture screen if the system is unable to perform an analysis when the Analyze button is pressed on the Capture screen. Service call or remote support is required to fix.
22	C	No data has been collected for either eye. Are you sure you wish to exit the Capture screen?"	Displayed on Capture screen if the operator pressed the Analyze/Save button without having collected any data on the capture screen.
23	C	Data has been collected for only one eye. Are you sure you wish to exit and analyze?	Displayed on Capture screen if the operator pressed the Analyze/Save button and has only collected data for one eye.
24	C	Are you sure you wish to discard the collected video?	Displayed on Capture screen if the operator clicked the Trash button in an attempt to discard the collected video.
25	C	Are you sure you wish to discard the collected image?	Displayed on Capture screen if the operator clicked the Trash button in an attempt to discard a collected still frame image.
26	E	The View Analysis screen is not configured correctly. Contact TearScience for technical support.	Displayed on View Analysis screen if it is unable to display the View Analysis sub-screen for a modality. Service call or remote support is required to fix.
27	E	An internal system error was encountered processing the data analysis. Consult the system log for details.	An internal system error was encountered during the processing of an analysis. Service call or remote support is required to fix.
28	E	An internal system error was encountered loading the analysis data. Consult the system log for details.	An internal system error was encountered attempting to load analysis data from disk into memory for display. Service call or remote support is required to fix.
29	E	The data storage disk space used has reached a critical level. Please perform a data archival operation. Image capture has been disabled until this problem is resolved.	Displayed on Capture screen when the data disk used space is greater than 95%. Further image capture has been disabled. Site administrator must either perform a system backup or delete some imaging sessions to gain free space.
30	I	The data storage disk space usage is above the warning threshold. Please perform a data archival operation when convenient.	Displayed on Capture screen when the data disk used space is above the warning threshold specified in the Backup/Restore Administration screen (default 75%). This message is to remind the operator to perform a backup in the near future.

ID	Type	Displayed Text	Description
37	C	There is unsaved data collected on the Capture Screen and the requested operation will discard this data. Are you sure you wish to proceed?	Displayed on Capture Screen if the operator attempts to exit the Capture screen with unsaved/unanalyzed data present.
38	E	The operating system encountered an error obtaining a list of drives on the system. Consult the system log for details.	Displayed when the Destination Drive list dialog is displayed but the system in unable to get a list of removable/networked drives from the operating system. Service call or remote support is required.
39	C	Please select one or more destinations for the output:	Displayed on the Destination Drive list dialog is displayed informing the operator of the intent of the drive list.
40	E	The output file '%1' is unable to be opened. The operating system error code is '%2'.	The system attempted to output a file of some type (e.g. video or still image) to an external USB or network drive and was unable to write the file. Check health and status of the storage location and try again.
44	I	No available drives are detected on the system.	Displayed by the Destination Drive dialog to inform the operator the system did not detect any external storage locations (either USB or networked).
54	E	An internal error was encountered accessing the notes database. Please contact TearScience for technical support.	The operator attempted to access the Notes Editor screen but a system internal error prevented the notes data from being accessed. Service call or remote is support required to fix.
55	C	Are you sure you wish to delete the selected note?	The operator has clicked the Delete Note icon and this message asks the operator to confirm the deletion.
56	C	Note information exists that has not been saved. Are you sure you wish to exit without saving the information?	The operator has entered text into a new note but has not clicked the Save Note button and is attempting to exit the Notes screen.
60	C	Please select the destination drive(s) for the exported images:	The operator clicked the Export Images button on the Export Screen and this message appears on the Destination Drive selection dialog to inform the operator of the function of the drive selection dialog.
62	E	An error was encountered producing the requested output. Please check the system log for details.	An internal system error occurred while producing export images or videos. Check the system log for more details. Service call or remote support is likely required.
63	E	An error was encountered producing the requested output. The error information from the operating system is '%1' (%2).	An error occurred with an external storage location in attempting to export images or videos to the storage location. Evaluate the error information given and resolve the problem. Examples of problems would be insufficient disk space to store the output, etc.
64	E	An error was encountered attempting to load the web page. The error information is '%2' (Code: %3).	An error occurred attempting to load a web page in the internal web browser (e.g. the Remote Support login screen). Attempt to access the page and ensure connectivity to the Internet.
76	C	Please select the destination drive(s) for the exported videos:	Displayed on Destination Drive selection dialog to prompt user to select destination for exported videos.
96	C	Data has not been collected for all eye and lid combinations. Are you sure you wish to exit the Capture screen?	Displayed on the Gland Image Capture screen if the operator has not collected image for both lids on both eyes.
109	C	Please select the destination printer for the report:	Displayed on the Printer Selection list when the operator chooses the Print Report feature from the Export screen.
110	E	The operating system encountered an error obtaining a list of printers.	The system was unable to get a list of printers from the operating system. Turn the device off then on again, and try to

ID	Type	Displayed Text	Description
		Consult the system log for details.	print the report again.
111	I	Video Data File Not Found On System	Displayed in the video pane of an analysis view screen if the source video file could not be located on the system or attached external storage.
112	I	Image Data File Not Found On System	Displayed in the still frame pane of an analysis view screen if the source image file could not be located on the system or attached storage.
113	C	Please select the destination drive for the PDF:	Displayed on the Drive Select list dialog after the operator has chosen to Save a PDF file of the report by touching the Save PDF button from the Export screen.
114	I	No printers are installed on the system	Displayed on the Printer Selection list dialog when no printers are installed on the system. Install a printer before attempting to print.
125	I	The entered password is not correct.	Displayed where an operator is required to enter a password and enters an incorrect password.
127	I	Please check the position of the chinrest and ensure it is in the rear position.	Displayed when the chinrest is not in the correct position for imaging.
128	I	The maximum number of images has been captured. To capture additional images, delete one or more of the existing images.	Displayed on the Ocular Image Capture screen when the operator has captured the maximum number of still images and then attempts to capture another.

Appendix: Electromagnetic Compatibility Requirements

Table 8: Guidance and Manufacturers Declaration-Electromagnetic Emissions

LipiView II is intended for use in the electromagnetic environment specified below. The customer or the user of LipiView II should assure that it is used in such an environment.		
Emissions Test	**Compliance**	**Electromagnetic Environment-Guidance**
RF emissions CISPR 11	Group 1	LipiView II uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment.
RF emissions CISPR 11	Class A	NA
Harmonic emissions IEC 61000-3-2	Class A	NA
Voltage fluctuations Flicker emissions IEC 61000-3-3	Complies	LipiView II is suitable for use in all establishments **other than** domestic and those directly connected to the public low-voltage power supply network that supplies buildings for domestic purposes.

Table 9: Guidance and Manufacturers Declaration-Electromagnetic Immunity (part 1)

LipiView II is intended for use in the electromagnetic environment specified below. The customer or the user of LipiView II should assure that it is used in such an environment.			
Immunity Test	**IEC 60601 Test Level**	**Compliance Level**	**Electromagnetic Environment-Guidance**
Electrostatic discharge (ESD) IEC 61000-4-2	±6 kV contact ±8 kV air	±6 kV contact ±8 kV air	Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%
Electrical fast transient/burst IEC 61000-4-4	±2 kV for power supply lines ±1 kV for input/output lines	±2 kV for power supply lines ±1 kV for input/output lines	Mains power quality should be that of a typical commercial or hospital environment
Surge IEC 61000-4-5	±1 kV differential mode ±2 kV common mode	±1 kV differential mode ±2 kV common mode	Mains power quality should be that of a typical commercial or hospital environment.
Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11	<5 % U_T (>95 % dip in U_T for 0,5 cycle 40 % U_T (60 % dip in U_T) for 5 cycles 70% U_T (30% dip in U_T) for 25 cycles <5% U_T (>95 % dip in U_T) for 5 sec	<5 % U_T (>95 % dip in U_T for 0,5 cycle 40 % U_T (60 % dip in U_T) for 5 cycles 70% U_T (30% dip in U_T) for 25 cycles <5% U_T (>95 % dip in U_T) for 5 sec	Mains power quality should be that of a typical commercial or hospital environment. If the user of the equipment requires continued operation during power mains interruptions, it is recommended that the equipment be powered from an uninterruptible power supply or a battery.
Power frequency (50/60 Hz) magnetic field IEC 61000-4-8	3 A/m	3 A/m	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment.
*NOTE: U_T is the a.c. mains voltage prior to application of the test level.			

Table 10: Guidance and Manufacturers Declaration-Electromagnetic Immunity (part 2)

LipiView II is intended for use in the electromagnetic environment specified below. The customer or the user of LipiView II should assure that it is used in such an environment.

Immunity Test	IEC 60601 Test Level	Compliance Level	Electromagnetic Environment-Guidance
			Portable and mobile RF communications equipment should be used no closer to any part of the LipiView II, including cables, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter. **Recommended Separation Distance**
Conducted RF IEC 61000-4-6	3 Vrms 150 kHz to 80 MHz	10 V	$d = [3.5/V1]\sqrt{P}$ $d = [3.5/E1]\sqrt{P}$ 80MHz to 800MHz $d = [7.0/E1]\sqrt{P}$ 800MHz to 2.5GHz
Conducted RF IEC 61000-4-3	3 Vrms 80 MHz to 2,5 GHz	3 V/m	Where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer and d is the recommended separation distance in meters (m). Field strengths from fixed RF transmitters, are determined by an electromagnetic site survey, [a] should be less than the compliance level in each frequency range. [b] Interference may occur in the vicinity of equipment marked with the following symbol: 

NOTE 1 At 80 MHz and 800 MHz, the higher frequency range applies.

NOTE 2 These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.

[a] Field strengths from fixed transmitters, such as base stations for radio (cellular/cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the LipiView II is used exceeds the applicable RF compliance level above, the LipiView II should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as re-orienting or relocating the LipiView II.

[b] Over the frequency range 150 kHz to 80 MHz, field strengths should be less than 3 V/m.

Table 11: Recommended Separation Distances Between Portable and Mobile RF Communications Equipment and LipiView II

LipiView II is intended for use in an electromagnetic environment in which radiated RF disturbances are controlled. The customer or the user of LipiView II can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and LipiView II as recommended below, according to the maximum output power of the communications equipment.

	Separation distance according to frequency of transmitter m		
Rated maximum output power of transmitter W	**150 kHz to 80 MHz** $d=[3.5/V_1]\sqrt{P}$	**80 MHz to 800 MHz** $d=[3.5/E_1]\sqrt{P}$	**800 MHz to 2,5 GHz** $d=[7/E_1]\sqrt{P}$
0,01	0.12	0.12	0.23
0,1	0.37	0.37	0.74
1	1.2	1.2	2.3
10	3.7	3.7	7.4
100	12	12	23

For transmitters rated at a maximum output power not listed above, the recommended separation distance *d* in meters (m) can be estimated using the equation applicable to the frequency of the transmitter, where *P* is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer.

NOTE 1 At 80 MHz and 800 MHz, the separation distance for the higher frequency range applies.

NOTE 2 These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.

APPENDIX H: LID WIPER EPITHELIOPATHY WORK AID

Lid Wiper Epitheliopathy Work Aid

Upper and Lower Lid Wiper Epitheliopathy (Lid Margin Staining) using Lissamine Green

Materials:

1. Lissamine green (LG) Green Glo strips (1.5mg strips)
2. Eyecept unpreserved saline
3. Cotton tipped swab/applicator

Background:

As shown in **Figure 1**, the sagittal height (width) of the lid wiper extends from approximately the inner border of the Line of Marx to the change in shape of the wiper surface approaching the subtarsal fold. In **Figure 1**, a thin line of fluorescein staining denotes Marx's line, which follows the irregular path of the row of meibomian gland orifices almost continuously along the mucocutaneous junction. Note that staining of the Line of Marx is a thin bright line and a normal finding, as contrasted to lid wiper epitheliopathy (LWE) staining which is typically wider and diffuse.

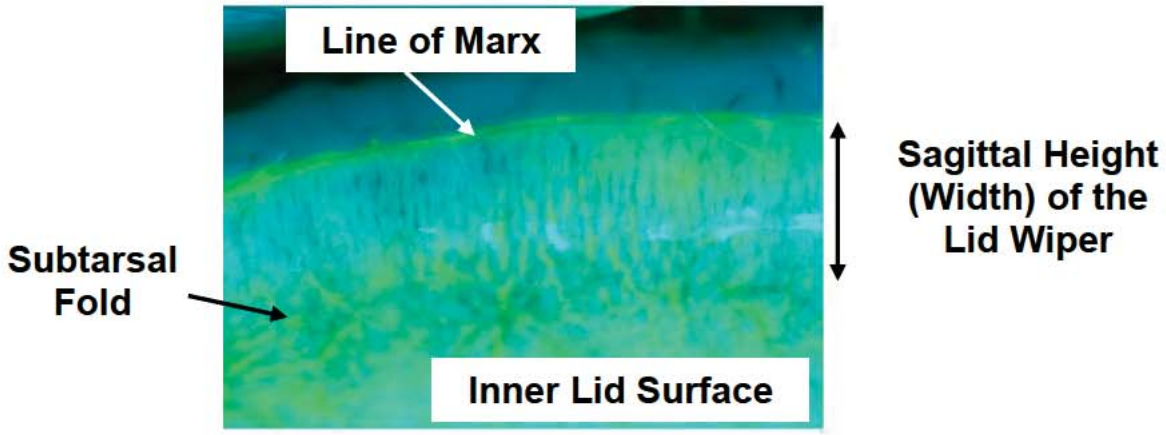


Figure 1: Sagittal Height (Width) of Lid Wiper from Line of Marx to Subtarsal Fold

- The ***horizontal length of the lid wiper*** extends from the superior punctum to the lateral canthus.
- The ***sagittal height (width) of the lid wiper*** extends from just proximal to the line of Marx to the subtarsal fold.

Procedure:

The Investigator assesses for LWE after instillation of lissamine green dye on the eye using the following method. Note that this method is similar to one previously published [1], but with the use of lissamine green instead of fluorescein and rose bengal, and the timings have been altered.

1. Apply one complete drop of unpreserved saline on one lissamine green strip. Note that the drop should traverse through air prior to contacting the strip to avoid partial drop application.
2. Let the saline soak into the strip for 3 seconds.
3. If present, remove the excess saline from the strip by shaking gently.
4. Optimal dye transfer may be achieved by contacting the palpebral or bulbar conjunctival as appropriate (below) with the wetted side of the dye strip. Additionally, care should be taken to achieve flat contact of

the dyed portion of the strip with the conjunctiva. The entire dyed length of the strip should contact the conjunctiva. Instill the dye to one of the following locations:

a. The inferior cul-de-sac of one eye if bulbar conjunctival staining is to be assessed as part of the protocol. If instilling the dye in this location take care that the lower lid wiper is not touched during instillation.

b. The superior bulbar conjunctiva if conjunctival staining is not going to be assessed as part of the protocol. If instilling the dye in this location take care that the upper lid wiper is not touched during instillation.

5. With a new dye strip, immediately repeat steps 1-4 for the same eye to complete a second strip dose for the first dye instillation.
6. Perform the next step after a wait time of 1 minute.
7. With two new dye strips, perform a second instillation of lissamine green dye by repeating steps 1 through 5. Note that four dye strips have been used for one eye.
8. Perform the next step after a wait time of 3 minutes.
9. Evert the lower eyelid of one eye with care to avoid contact with the lid wiper.
10. Evaluate the lower lid margin under white light, 10X magnification recommended.
11. Examine the entire horizontal length of the lid wiper from the punctum to the lateral canthus. Preferred method of grading of length in mm is via slit lamp reticle, but slit beam length may also be used if needed. Grade the horizontal length of staining observed to the nearest mm as shown in Table 1 on a scale of 0 to 3. Note that if there are separate areas of staining along the entire horizontal length of the lid wiper, sum the areas together to determine the grade. Document the horizontal length staining grade.

Table 1: Horizontal Length of Lid Wiper Grading Scale	
GRADE	**HORIZONTAL LENGTH OF STAINING**
0	< 2 mm
1	2 ≥ to < 4.5 mm
2	4.5 ≤ to < 9.5 mm
3	≥ 9.5 mm

12. Examine the entire sagittal height (width) of the lid wiper from proximal to the line of Marx to the subtarsal fold. Grade the sagittal height of staining observed based on the percentage of staining over the width of the lid wiper, as shown in Table 2 on a scale of 0 to 3. Note that if there is a range of staining along the width of the lid wiper, estimate the average width to determine the grade. Document the sagittal height staining grade.

Table 2: Sagittal Height (Width) of Lid Wiper Grading Scale	
GRADE	**SAGITTAL HEIGHT (WIDTH) OF STAINING**
0	< 25%
1	25% to < 50%
2	50% to < 75%
3	≥ 75%

13. Repeat steps 9 through 12 on the upper lid.

14. If eyelid photography is indicated, follow the steps in Appendix A. Repeat all of the above steps for the for the fellow eye.

Grading:

	OD		OS	
Area	Upper Lid (UL)	Lower Lid (LL)	Upper Lid (UL)	Lower Lid (LL)
Horizontal				
Sagittal				

Note that there is no averaging of the grading. There will be 8 LWE grades recorded per subject evaluation. For reference, a photographic example of horizontal length and sagittal height grading of the lid wiper under lissamine green staining is shown in **Figure 2**.

The horizontal length of lissamine green staining on the lid wiper is observed in two sections (between the two white and two black lines) and when combined the total length is over 10 mm long, which is scored as Grade 3. The staining of the sagittal height (width) of the lid wiper shows a range of widths (between the two sets of black arrows) that is estimated to be an average of 25% to <50% across all stained areas of the lid wiper and is scored as Grade 1.

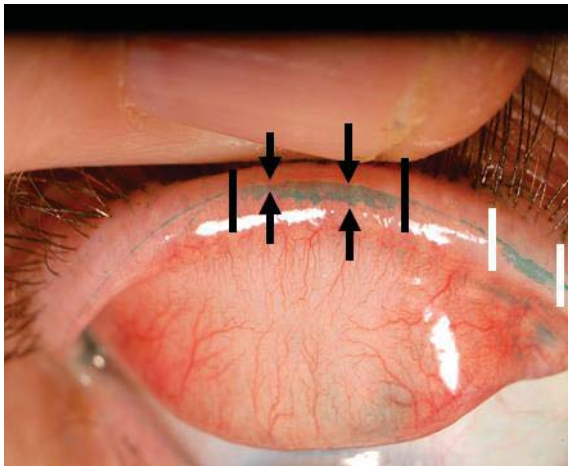


Figure 2: Photographic Example of LWE Grading

REFERENCES

1. Korb DR, Herman JP, Greiner JV, et al. Lid wiper epitheliopathy and dry eye symptoms. *Eye & Contact Lens* 2005:31:2-8.
2. Efron N, Brennan NA, Morgan PB, et al. Lid wiper epitheliopathy. *Progress in Retinal and Eye Research* 53(2016) 140-174.

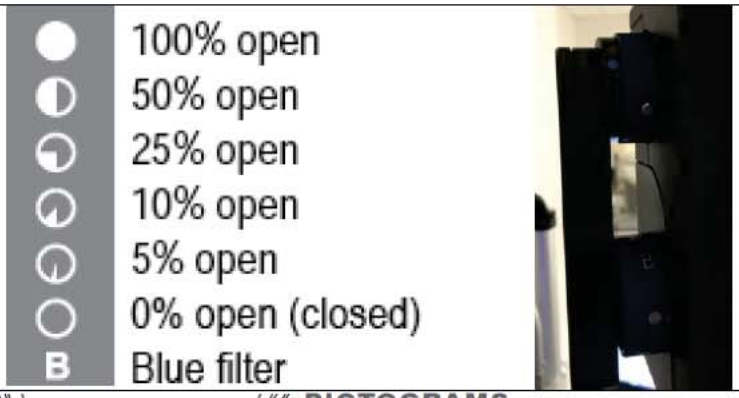
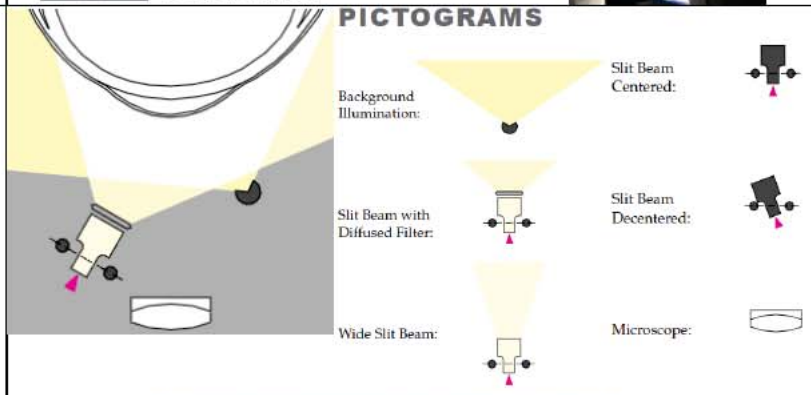
1. Please review the Light Toxicity section in the BX900 manual. Note that the daily limit is 90 pulse flashes per day (each photograph is one pulse flash). Note that the daily limit of LED illumination used for the slit and background illumination depends on the intensity set (Step 8).

LED Illumination Intensity	Daily Limit [minutes]
1	15.00
2	7.50
3	5.00
4	3.75
5	3.00
10	1.50

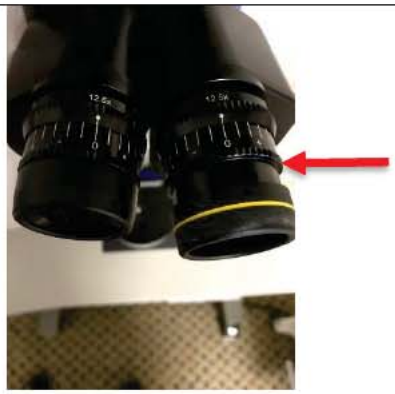
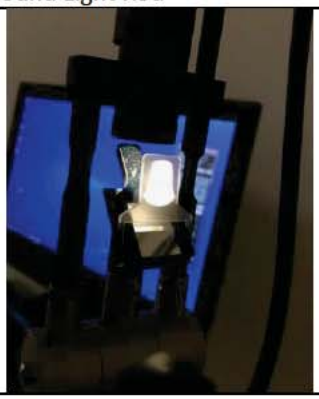
2. Turn on the Slit Lamp in the following order:
   A. Green switch on table.
   B. Computer, bottom right corner button.
   C. Camera body, top left corner.
   D. Green switch on flash source on when ready to acquire images.

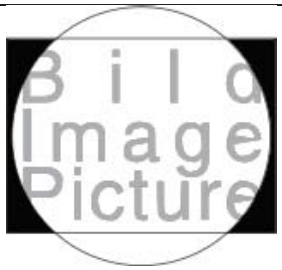
3. Set up patient information in EyeSuite program.

4. Set the flash intensity on LOW, if it is not already set to LOW (top right switch, bottom pushed down).

5. 100% open background illumination (bottom knob) with white light (top knob).	
6. 30-45°Angle between microscope and background illumination. 7. Angle between microscope and slit beam 30°–45°	
8. Adjust the background and slit beam light intensities as desired for photography focus and field of view optimization. Note that neither of the knobs pictured at the right contribute to the photography illumination, so they should be set to a minimum and below the daily safety limit requirement.	
9. Slit beam vertical and fully open (slit width and height)	

10. Magnification 6.3X 11. Recommended aperture: 2. Note that lower apertures allow more light for photography, but reduce the depth of focus.	
12. Recommended shutter speed: 4 (1/60). Note that a longer shutter speed will allow more light for photography but may result in a motion blurred image. 13. Recommended sensor rating ISO 1000. Note that ISO sensitivity can be increased to brighten the image.	
14. Remove background light rod and insert test rod.	 Background Light Rod  Test Rod
15. Examiners who do not wear glasses: Pull the occluders out as far as they will go. Examiners who do wear glasses: Push the occluders in as far as they will go. Each eyepiece should be set individually by turning the knurled ocular refraction ring.	Occluder In  Occluder Out

16. Focus crosshair on test piece by rotating the ocular refraction ring on the right eye piece. This setting is performed from the (+) side to the (-) side at low magnification until the double crosshair comes into sharp focus. Note: The 12.5x eyepiece with double cross hair reticule is only in the right ocular of the microscope. This must be correctly focused for the user's eye to ensure sharp images are captured. This setting is not the user's refractive error.	
17. Remove test rod and re-insert background light rod. Ensure polarizer cap is attached to background light rod if use of crossed polarizers is desired.	 Background Light Rod  Test Rod
18. Diffused filter on. Ensure polarizer cap is attached to the diffuser if use of crossed polarizers is desired.	
19. When aligning the slit lamp to the subject, note that the background illumination post is in place to avoid contacting the subject's nose. The subject may need to turn their head slightly to move their nose away from the background illumination post.	
20. Evert the subject's lower lid using two fingers, trying to pull both sides of the lid down so the	

entire stain corner to corner is visible. Ensure that the fingers are low and flat enough so they do not cast a shadow on the lid.	
21. Center the camera optimally such that edge to edge of the lid is within the field of view (FOV). Note the difference in field of view between eye piece and acquired image (acquired image has larger FOV horizontally than eye piece).	 Circle: The field of view of the object observed through the microscope's eyepiece. Rectangle: Area of photograph.
22. If using the specular reflection reduction cross polarizer system is desired, rotate the polarizer until the specular reflection is minimized.	
23. Ensure the entire LWE stain from corner to corner is within the field of view and is in focus. Ensure that the crosshair is also in focus. Capture Image by pressing blue bar on base of unit.	
24. Review the image that is presented on the computer monitor. Verify that the field of view includes the LWE stain from corner to corner and the entire stain is in focus. Acquire 3 images for the lower lid. Repeat above steps and acquire 3 images for the upper lid.	

APPENDIX I: MEIBOMIAN GLAND EVALUATOR

Meibomian Gland Evaluator
Model MGE-1001 Package Insert - English

Meibomian Gland Evaluator Device Description:

The Meibomian Gland Evaluator is a handheld instrument used by a physician to evaluate Meibomian gland secretions in adult patients during a routine eye examination. The instrument provides a standardized method to apply consistent, gentle pressure to the outer skin of the lower eyelid while visualizing the secretions from the Meibomian gland orifices through a slit lamp biomicroscope. The pressure applied to the eyelid when using the device is between 0.8 g/mm^2 and 1.2 g/mm^2.

Directions for Use:

Assess the Meibomian glands in the three regions under the eyelid: temporal, central and nasal. Approximately five glands are expressed per region with each use of the Meibomian Gland Evaluator.

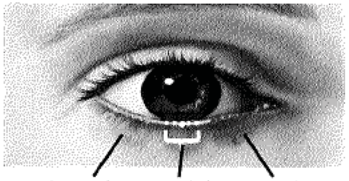


Figure 1: Eyelid Gland Regions

Meibomian Gland Evaluation - Step by Step:

1. Prior to initial use of the Meibomian Gland Evaluator, check for any rough surfaces that may come in contact with a patient's eyelid.
2. Wash your hands and disinfect the Meibomian Gland Evaluator with alcohol prior to use on each patient.
3. Under the slit lamp at 10x-16x magnification, locate the lower eyelid and gland regions. (Figure 1).

Starting with the temporal region:

4. Instruct the patient to look upwards. Avoid any contact of the instrument with the eye.
5. Holding the Meibomian Gland Evaluator between your forefinger and the thumb, place the shaft to the skin immediately below the lash line of the lower eyelid so that the long dimension is parallel to the eyelid margin.
6. Once full contact is achieved between the contact surface and the outer surface of the lower eyelid, rotate the shaft of the instrument downward approximately 15 to 45 degrees so that the leading face is tangential to the eyeball.

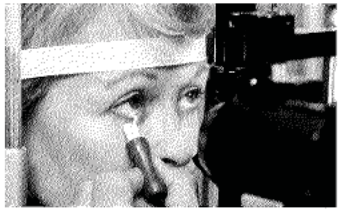
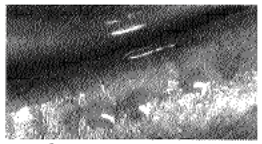


Figure 2: Meibomian Gland Evaluator Placement

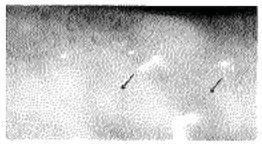
7. Depress the shaft of the instrument mid-way (approximately 3mm) to exert a constant force on the meibomian glands. Adjust the position of the instrument to cause the flat surface of the lower eyelid margin to roll slightly outward for a clear view of the Meibomian gland orifices.
8. To facilitate observation of the gland secretions, gently wipe clean the gland orifices along the eyelid margin with a cotton swab immediately after applying pressure and while holding the instrument in position and maintaining pressure.
9. Hold the instrument in place over the Meibomian glands for approximately 10-15 seconds while evaluating the secretion characteristics from each Meibomian gland.
10. Assess 5 consecutive glands in the center of the Meibomian Gland Evaluator
11. Repeat steps 4-9 for the central and nasal regions. (Figure 1)
12. Refer to the Secretion grading scale below to grade secretions for each of the 5 glands selected within the three regions (temporal, central and nasal). Record the grades for a total of 15 glands on the patient's chart. Next, calculate the Total Meibomian Gland Secretion Score by adding the grades for the 15 glands assessed. Record this score on patient's chart.
13. Disinfect the instrument with alcohol after each use.

Meibomian Gland Secretion Grading Scale:

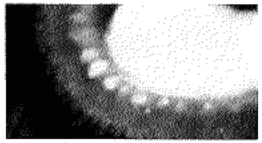
Grade	Secretion Quality
3	Clear Liquid Oil
2	Colored/Cloudy Liquid
1	Inspissated (semi-solid, toothpaste-like consistency)
0	No Secretion (Includes capped orifices)



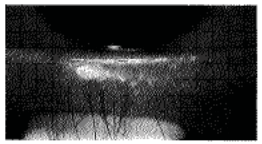
Grade 3: Clear Liquid Oil



Grade 2: Colored/Cloudy Liquid Oil



Grade 1: Inspissated



Grade 0: No secretion

Contraindications:
No contraindications are known.

Precautions:
Do not depress the shaft to the endpoint of the spring. Do not apply any additional force after the shaft has been depressed approximately 6 mm. Applying additional force negates the benefit of using the instrument to apply a standard force. Familiarity with use of a slit lamp biomicroscope is required to use Meibomian Gland Evaluator for assessment of the meibomian gland secretions.

Warnings:
To ensure proper use of the Meibomian Gland Evaluator, review the warnings below.

- Federal law restricts this device to sale by or on the order of a licensed physician.
- Do not use Meibomian Gland Evaluator if the package is open or broken. Do not use Meibomian Gland Evaluator if it appears broken or has sharp edges or rough surfaces upon initial inspection.
- Maintain proper infection control procedures including cleaning hands before handling the device and before evaluation of each patient. Disinfect the instrument with alcohol after each use and between patients.
- Avoid contact of the device with the eye. Instruct the patient to look up and away to avoid injury to the cornea in the event the contact surface inadvertently touches the eye.

Adverse Effects:
Potential adverse effects that are unlikely but may occur with use of the Meibomian Gland Evaluator include but are not limited to:

- Skin abrasion (e.g., from rough surface on the device)
- Eye abrasion (e.g., from improper contact of the instrument with the eye)
- Infection of the skin or eye (e.g., from improper or lack of disinfection after use and betweeen patients)
- Allergic or toxic reaction (e.g., from exposure to any residue on device during user handling)

Label Symbol	Symbol Description
REF	Reference number
LOT	Lot number
	Do not use if package is opened or damaged
Rx only	Federal law restricts this device to sale by or on the order of a licensed physician.
CE	This product conforms to EU consumer safety requirements.
EC REP	Authorized representative in the European Community
	Manufacturer
	Date of manufacture
	Consult operating instructions

Contents: Qty Description

1 Meibomian Gland Evaluator
Model MGE-1001

CE

EC REP Donawa Lifescience Consulting
Piazza Albania, 10
00153 Rome, Italy

TearScience

5151 McCrimmon Parkway
Suite 250
Morrisville, NC 27560 USA
Phone: (919) 467-4007

Covered by one or more of the following US patents, and other pending US and foreign patents: http://tearscience.com/patents

011807 (Rev B) September 15, 2015

JJVC CONFIDENTIAL

PROTOCOL COMPLIANCE INVESTIGATOR(S) SIGNATURE PAGE

Protocol Number and Title: CR-6332 Ocular Characteristics in Contact Lens and Spectacle Wear
Version and Date: 4.0 16 April 2019

I have read and understand the protocol specified above and agree on its content.

I agree to conduct this study according to ISO 14155,[1] GCP and ICH guidelines,[2] the Declaration of Helsinki,[3] United States (US) Code of Federal Regulations (CFR),[4] and the pertinent individual country laws/regulations and to comply with its obligations, subject to ethical and safety considerations. The Principal Investigator is responsible for ensuring that all clinical site personnel, including Sub-Investigators adhere to all ICH[2] regulations and GCP guidelines regarding clinical trials during and after study completion.

I will assure that no deviation from, or changes to the protocol will take place without prior agreement from the Sponsor and documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial participants.

I am responsible for ensuring that all clinical site personnel including Sub-Investigators adhere to all ICH[2] regulations and GCP guidelines regarding clinical trials during and after study completion.

All clinical site personnel involved in the conduct of this study have completed Human Subjects Protection Training.

I agree to ensure that all clinical site personnel involved in the conduct of this study are informed about their obligations in meeting the above commitments.

I shall not disclose the information contained in this protocol or any results obtained from this study without written authorization.

Principal Investigator:

_____ _____
Signature Date

_____
Name and Professional Position (Printed)

Institution/Site:

_____
Institution/Site Name

_____
Institution/Site Address